AN OPEN COMPARATIVE CLINICAL EVALUATION ON "UTHIRAVADHA SURONITHAM (RHEUMATOID ARTHRITIS)" WITH SIDDHA HERBAL – MINERAL FORMULATION DRUG "SAMUTHARA CHOORANAM"(INTERNAL), "VADHA NOIKU VELIPRAYOGHA THAILAM"(EXTERNAL) & OTTRADAM

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **An open comparative clinical evaluation on "Uthiravadha suronitham (Rheumatoid arthritis)" with siddha herbal – mineral formulation drug "Samuthara Chooranam" (Int), "Vadha Noiku Veliprayogha Thailam" (Ext) & Ottradam** is a bonafide and genuine research work carried out by me under the guidance of **Prof. Dr. M. MOHAMED MUSTHAFA, M.D(S),** Post Graduate Department of **Sirappu Maruthuvam**, Govt. Siddha Medical College, Arumbakkam, Chennai-600106 and the dissertation has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

Date: **Signature of the Candidate**

Place: Chennai **Dr. A. B. KAVINAYA**

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CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **An open comparative clinical evaluation on "Uthiravadha suronitham (Rheumatoid arthritis)" with siddha herbal – mineral formulation drug "Samuthara Chooranam" (Int), "Vadha Noiku Veliprayogha Thailam" (Ext) & Ottradam** is submitted to the Tamilnadu Dr. M.G.R. Medical University in partial fulfillment of the requirements for the award of degree of M.D (Siddha) is the bonafide and genuine research work done by **A. B. KAVINAYA** under my supervision and guidance. The dissertation has not formed the basis for the award of any Degree, Diploma, and Associate ship, Fellowship or other similar title.

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ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **An open comparative clinical evaluation on "Uthiravadha suronitham (Rheumatoid arthritis)" with siddha herbal – mineral formulation drug "Samuthara Chooranam"(Int), "Vadha Noiku Veliprayogha Thailam"(Ext) & Ottradam** is a bonafide work carried out by **A. B. KAVINAYA** during the year 2015-2018 under the guidance of **Prof. Dr. M. MOHAMED MUSTHAFA, M.D (S),** Post Graduate Department of Sirappu Maruthuvam, Govt. Siddha Medical College, Chennai - 600 106.

Seal & Signature of the HOD **Seal & Signature of the Principal**

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Place: Chennai **Place:** Chennai

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CONTENTS

INTRODUCTION

1. INTRODUCTION

Siddha system of medicine is one of the long-lived traditional system which is gradually evolved along with Dravidian's culture and hence this system is known as Dravidian system of medicine. This system was contemporaneous with those of the submerged lands, Egyptian, Mesopotamian, Chinese and Greciam medicine.

The unique nature of this medicine is the continuous service to humanity for more than 5000 years in combating diseases and in maintaining physical, mental, moral and spiritual components of human beings and to make the body perfect, imperishable, hence to promote longevity.

This is the ancient synthetic chemico – philosophical system, which deals with **1.Vada(Alchemy) 2.Vaidhya(Medicine) 3.Gnanam(Wisdom) and 4.Yoga**

1. Alchemy – chemistry which deals and treats of transforming in clear lucid fashion in all its branches of changing baser metals to higher by minerals, vegetables and animals.
2. Vaidhya – is that of medicine by chemistry for the ailments of man.
3. Gnana – is the study of nature, matter, soul and of man and human society and the scientific modulation of man and universal god.
4. Yoga – is the practice of Brahma vidya or Raja yoga to attain the "Moksham"

Siddha system has unique art of healing founded by great spiritual scientist called **"SIDDHARS"**. The term SIDDHAR has derived from the word **'SIDDHI'** which literally means accomplished, achieved or success and so it refers to one who had attained his end in spiritual goal by focusing Eight Supernatural Power **"Ashtamaha Siddhi"**.

They belong to the class of **EIGHTEEN SUPERNALS** or **DEMIGODS** inhabiting the middle air and embracing several subdivisions, hence the following proverb is applicable only to them.

"THERE IS NO GREY HAIR NOR WRINKLE AND NO DEATH"

Siddhars, the followers of **LORD SHIVA** where **AGASTHIAR** being the first siddhar. Along with SRI LOBHA MATHA DEVI, he adorns the first and foremost peedam(seat) of the siddhas.

THIRUMOOLAR, the prince of mystics was one of the disciples of Nandhi Dever. The 3000 stanzas(Poems) delivered by him during the course of 300 years what is today known as **"THIRUMANTRAM"**.

Thirumantram deals with body as well as soul. It is concerned with human anatomy as well as human mind.

"IF THE BODY IS DESTROYED, LIFE IS DESTROYED;
NOR WILL LIFE COME BY TRUE WISDOM FIRM;
KNOWING MEANS, THE BODY TO FOSTER,
I FOSTER THE BODY AND THUS THE LIFE"

Which means the body is as important as the soul. Divorced from the body the soul is naught.

According to the siddhar **'YUGI MUNI'**, the diseases are classified into 4448 based on derangement of **Vadha, Pitha and Kabha**.

The disease "UTHIRAVADHA SURONITHAM" are brought under the types of vadha diseases. Here the clinical features of **'RHEUMATOID ARTHRITIS'** are correlated with **"UTHIRAVADHA SURONITHAM".**

Rheumatoid arthritis is a generalized chronic multisystem disease affecting the connective tissues of the whole body with focalized involvement of musculoskeletal system. It is considered to be an autoimmune response to an unknown antigen and antibody formed is rheumatoid factor which is identified as IgM.

About 1% of world population is affected by RA. In adult Indian population, prevalence rate is 0.75%. 80% womens were affected. Womens 2 to 3 times more common than males. Male Female ratio is 1:3. Most often occur in 25 - 50 years of age.

Since RA is a chronic disease, NSAID drugs are used in modern medicine to reduce the pain and inflammation but do not slow down the progression of joint damage. Recently approved **DMARD Leflunomide**, **an Immunomodulator drug** have high potential effect on managing the signs and symptoms of RA but it shows some side effects like alopecia, diarrhoea, elevated liver enzymes and allergic rashes.

In siddha system of medicine, thousands of raw drugs are used in the treatment of diseases. These drugs are catagorised into 3 groups namely Metals, Minerals, Herbals and Animal products. More than 80% of medicines are formulated by herbal products.

But in certain life threatening diseases and in many chronic diseases, the herbal medicines alone have not been much effective. In such conditions, siddhars enumerated some Herbo – metal and Herbo – mineral formulations.

For this reason I chosen the siddha trail medicine Herbal – Mineral formulation drug **"SAMUTHARA CHOORANAM" (Internal)** which have **IMMUNOMODULATOR ACTIVITY** in its ingredients and **"VADHA NOIKU VELIPRAYOGHA THAILAM" (External)** along with **"OTTRADAM" (Therapy)** for the study of **'UTHIRAVADHA SURONITHAM'**

Hence my study goal is to evaluate whether the trial drug **Samuthara Chooranam(Internal)** along with External medicine and Ottradam(Therapy) is **Efficacy** and **Safety** for the disease **Uthiravadha Suronitham(RA).**

AIM AND OBJECTIVES

2. AIM AND OBJECTIVES

AIM:

To Study the safety and the therapeutic efficacy of Siddha medicine "Samuthara chooranam" (Internal) and "Vadha noiku veliprayogha thailam" (External) and "Ottradam"(Therapy) in "Uthiravadha Suronitham"(Rheumatoid arthritis)

OBJECTIVES:

PRIMARY OBJECTIVE:

To study the safety and therapeutic efficacy of siddha medicine in "Samuthara chooranam"(Internal) and "Vadha noiku veliprayogha thailam"(External) and "Ottradam"(Therapy) in "Uthiravadha suronitham"(Rheumatoid arthritis).

SECONDARY OBJECTIVE:

1.To collect the various siddha literature and modern literature regarding the disease Uthiravadha suronitham(Rheumatoid arthritis)

2.To use modern parameters to confirm diagnosis, severity of the disease and progress of the disease.

3.To explore the traditional preparations with scientific evaluation of trial drug.

4.To evaluate the physico-chemical analysis of siddha trial drug "Samuthara chooranam".

5.To evaluate the pharmacological and safety standard of trial drug in animal models.

6.To evaluate the efficacy of the trial drug in Rheumatoid patients in terms of pain assessment score before and after treatment.

7.To evaluate the therapeutic efficacy of external therapy "Ottradam" in Rheumatoid patients.

8.To evaluate the safety parameters of the siddha trial drug in Rheumatoid patients in terms of liver function and renal function test before and after treatment.

REVIEW OF LITERATURES

3. REVIEW OF LITERATURE

3.1. SIDDHA ASPECT

Man according to siddha system is production of divine mind and thought produced essence of the five elements, sole of the stars, and the spirit which is the stellar and temporal sides of magnum limbus from the matrix of nature formed of seven layers of tissues.

These five elements together constitute the human body and origin of other material objects are explained as Pancheekaranam (Mutual Intra Inclusion). None of these elements could act independently by themselves. They could act only in coordination with other four elements. All the living creatures and the non-living things are made up of these five basic elements. The five basic elements form the connecting link between the Microcosm (Man) and Macrocosm (World). Any change in the universe due to natural or unnatural causes will create changes in human systems.

"நிலம் நீர் தீ வளி விசும்போ டைந்தும்

கலந்த மயக்க முலகமாதலின்"

- தொல்காப்பியம் பொருள் அகராதி

Again it is said, like the universe man is composed of five elements such as earth, water, air, fire, ether. Therefore life force is the basis for man's mental and spiritual activities on that nature may evolve him towards perfection.

- The earth gives shape to the body and release Sits energy, Bones, muscles, and tissues represent if in the body.
- Water makes the earth supple and helps in the transmission of energy, serum, lymph, saliva etc.. represent it in the body.
- Fire makes the form of the body steady and gives vigour and stimulation. Digestion and circulation represent it in the body.
- Air ignites the fire and works as a life carrier and is the support of all contact and exchange. Respiration and Nervous system represent it in the body.
- Ether is the creator of life itself in the body. A harmonious combination and function of these elements in the body produce a healthy and beautiful life.

THE 96 BASIC PRINCIPLES (96 Thathuvam)

According to Siddha system of medicine, 'Thathuvam' is considered as a science that deals with basic functions of the human body. Siddhars described 96 principles as the basic constituents of human body that include physical, physiological, psychological and intellectual components of an individual. These 96Thathuvams are considered to be the cause and effect of our physical and mental well-being. The Thathuvam is the author of the conception of human embryo on which the theory of medicine is based.

There are in our body several supports to the soul for the existence and sustenance of life and they are the five elements (Earth, Water, Fire, Air, Ether), the six plexus, the three humors (mukkuttram), 72,000 blood vessels and nerves etc.. Constituting in all 96 thathuvas.i.e constitute principles in nature. These three humours (vatham, pitham, kabham) plays a major role in the body and their function remain in the balanced state in a normal healthy person and disturbance in their equilibrium leads to the development of diseases in the body.

If the siddha medicine is to accomplish its real mission it must start a double movement of revival and reform. It must to revive its tridoshic theory on which the whole ancient medicine is based.

"முப்பிணி மருவி முனிவுகொள் குறிப்பைத்
தப்பாதறியும் தன்மையும் வாத
பித்தவையம் பிரிவையும் அவைதாம்
ஏறியிறங்கி இணைந்துக் கலந்து
மாறிமாறி வரும் செயற்கையார் பிணி
நேர்மையறிந்து நீட்டு மருந்தே
சீரியதாமெனச் செப்புவர் சித்தரே"

- நோய் நாடல் நோய் முதல் நாடல் திரட்டு

Man develops three distinct, personalities namely the mind and the vital or life force and the body. Through the mind he thinks and wills; through the vital or life force he executes his thought and will; through the physical body he expresses what he thinks and wills. The mind is vatha, vital or life force is Pitha, and the body is kabha.

- Vatha, pitha, kabha have multiple significances and symbolical in terms.
- Vatha represents Vayu, mind, dryness, pain, flatulence, sensitiveness, lightness, and also air.
- Pitha represents gastric juice, bile energy heat, inflammation, anger and irritation, etc...
- kabha represents feeling of cold, heaviness, running of the nose, passing mucoid discharge and also the saliva.

They are also formed by the combination of the five basic elements. Accordingly Vali is formed by the combination of Vali (Air) and Aagayam (Space). This is the Creative force. Azhal is formed by Thee (Fire). This is the Force of Preservation. Iyyam is formed by Mann (Earth) and Neer (Water). This is the Destructive Force. These three humours are in the ratio 4:2:1 in equilibrium which is a healthy normal Condition. They are called as the life forces or humours.

THE FORMATION OF UYIR THATHUKKAL:

1.The Valinaadi is formed by the combination of Abanan and Idagalai.

2.The Azhalnaadi is formed by the combination of Piranan and Pinkalai.

3.The Iyyanaadi is formed by the combination of Samanan and Suzhumunai.

- Vaatham - Ten types
- Pitham - Five types
- Kabam - Five types

(a) Five forms of vadha:

These are the five main centres of the subtle physical body and correspond to the nervous plexuses of the gross physical body.

- **Matedial of muladhar centre (அபானன்):** This centre corresponds to the pelvic plexus and is the seat of kundalini or material energy and controls excretions
- **Navel centre (சமானன்):** This corresponds to the solar plexus in the navel region and controls digestion.
- **Heart centre (பிராணன்):** This refers to the cardiac plexus in the Heart and circulation.

- **Throat Centre (உதானன்):** This corresponds to the pharyngeal plexus in the throat region and control breathing and speech.
- **Forehead centre (வியானன்):** This corresponds to the Naso-ciliary plexus at the root-of the nose and base of the skull and control "will".

(b) Five forms of pitha:

- **Gastric juice (பாசகம்):** This give appetie and helps Digestion.
- **Bile (பிராசகம்):** which gives complexion to the skin.
- **Haemoglobin (இரஞ்சகம்):** which colours the blood.
- **Aqueous Humour (ஆலோசகம்):** Which brightens the eyes
- **Life energy (சாதகம்):** Which controls the whole body
-

(c) Five form of kapha:

- **Saliva (கிலேதகம்):** Which helps mastication
- **Cerebrospiral fluid (தற்பகம்):** Which keeps the head cool
- **Lymph (போதகம்):** Which gives taste
- **Serum (அவலம்பகம்):** Which helps the Heart in pumping
- **Synovial fluid (சந்திகம்):** Which lubricate and aids free movement of the joints

The three humours of vatha, pitha and kapha which are absorbed and circulated in the blood have each certain definite qualities: What are they actually,

1. VADHA.

(Own qualities-6)-	**(Opposite qualities-6)-**
Vatha is dry - வறட்சி	Unctuous - பசுமை
Vatha is cold - குளிர்ச்சி	Hot -அக்கினி
Vatha is subtle - அணுத்துவம்	Solid - கெட்டி
Vatha is rough - கடினம்	Soft - மிருது
Vatha is unstable - அசைதல்	Stable - ஸ்திரம்
Vatha is light - இலகு	Heavy - பளுவு

All this qualities are present in Air and hence air we inhale is Vadha

2. PITHA

(Own qualities-6)-	(Opposite qualities-6)-
Pitha is hot - அக்கினி	Cold - குளிர்ச்சி
Pitha is acid - புளிப்பு	Sweet - இனிப்பு
Pitha is mobile - பசுமை	Immobile - நிலைதிருத்தல்
Pitha is liquid - சலரூபம்	Solid - கெட்டி
Pitha is acute - குரூரம்	Mild or harmless - சாந்தம்
Pitha is pungent - காரம்	Bitter - கசப்பு

All this qualities are present in the gastric juice and hence the gastric juice is Pitha

3. KAPHA

(Own qualities-6)-	(Opposite qualities-6)-
Kapha is cold – குளிர்ச்சி	Hot - உட்டிணம்
Kapha is heavy - பளுவு	Lite - இலகு
Kapha is immobile - அசைவின்மை	Mobile - அசைதல்
Kapha is sweet - இனிப்பு.	Pungent - காரம்
Kapha is soft - மிருது	Rough - கடினம்
Kapha is unctuous - ஈரம்	Dry – வறட்சி
Kapha is viscid - வழவழப்பு	Sandy - கரகரப்பு

All this qualities are present in in Saliva so Saliva is Kapha

VADHAM:

The term Vadham denotes Vayu, pain, dryness and flatulence. Vadham is responsible for respiration and control of all movements.

Location -Abanan, Faeces, Idakalai, Pelvic bone, spermatic cord, skin, nerves, joints, hairs and muscles.

Character -It governs the other two basic elements and responsible for all physical process in general. For this reason, disturbance in vadha tend to have more severe implication than the other two humours and other affect the mind as well as entire physical body and also responsible for respiration.

Functions -Pain in the whole body, twitching, pricking pain, inflammation, reddish complexion, and roughness of skin, hardness of limbs, astringent sense of taste in the mouth, constipation, and oliguria, blackish discoloration of skin, stool, urine and muddy conjunctiva.

So for 4448 diseases are classified by **Agasthiyar rathina surukkam naadi** and in this **Vadha diseases** are classified as 84 types

"நாளடா நாற்பத்து நாலு நூறு

நயமுடனே நாற்பத்து எட்டு ரோகம்

பாரப்பா வாதமது எண்பத்து நாலு"

Vadham or vali is not mere wind, but also that causes motion, energy, and sensation of every cell in the body. Vali relates to the nerve force. It is responsible for all movements in the mind and the body.

In human body the locomotors activity functions through voluntary muscles and its activities controlled by nerves system called Kanmendhriyam, likewise the sensation and its activities are known as Gnanendhriyam. These types of activities are governed by valikutram among the mukkutram.

LOCATION OF VADHA HUMOUR:

- Below the navel region (umbilicus)
- Urinary bladder, motion, Spermatic cord, Umbilical cord, thigh, bone, skin, nerves, joints, muscles, hair follicles, pelvis, ear.
- வாதத்தின் இருப்பிடம்: **பெருங்குடல்.**

NATURAL PROPERTIES OF VADHAM:

"ஒழுங்குடன் தாதேழ் மூச்சோங்கி இயங்க

எழுச்சிபெற எப்பணியு மாற்ற எழுந்தரிய

வேகம் புலன்களுக்கு மேவச் சுறுசுறுப்பு

வாகளிக்கும் மாந்தர்க்கு வாயு"

-மருத்துவ தனி பாடல், சித்த மருத்துவாங்க சுருக்கம் (பக்கம் 140)

- Functioning of mind throughout the body
- Giving briskness
- Making the uniform functioning of seven udalkattugal
- Protection and strengthening of five sensory organs.
- Regulation of fourteen physiological reflexes.

QUALITIES OF VADHAM:

"வாதங் கடுமை வறட்சியுடன் நொய்மை

சீதமுஞ்ச் சலனம் சிதறணுவு ஏதமுட

னிக்குணத்தோடுற் றேயியக்கந்த ருமளவிற்

தக்க பரிகாரந்தா"

- **கண்ணுசாமியம் (பக்கம் 21)**

Own qualities-6

Vadha is dry - வறட்சி

Vadha is cold - குளிர்ச்சி

Vadha is subtle - அணுத்துவம்

Vadha is rough - கடினம்

Vadha is unstable -அசைதல்

Vadha is light - இலகு.

"வாத குணமாறுக்கு மாறுகுணமே னோக்கின்

ஒதமிரு தீரம் உயிர்பாரம் பேராதரவோ

யுள்ள தீயோடுறதி யியற்றுத் திரளாக

உள்ள குணத்தையே ஊட்டு.

- **கண்ணுசாமியம்- பக்கம்-22**

(Opposite qualities-6)

Unctuous - பசுமை

Hot - அக்கினி

Solid - கெட்டி

Soft - மிருது

Stable - ஸ்திரம்

Heavy - பளுவு

VARIETIES OF VADHAM:

"முறையாம் பிராணனோட பானன் வியானன்
மூர்க்கமா முதோனனொடு சமான னாகும்
திறமையாங் கூர்ம னோடுகிருகிர ன்றோன்
தேவத் தனோடு தனஞ்செயனு மாகும்."

- சித்த மருத்துவாங்க சுருக்கம் பக்கம்-142

VAAYU – 10 (VITAL NERVE FORCE WHICH IS RESPONSIBLE FOR ALL KINDS OF MOVEMENTS)

1.Uyirkaal (Piraanan)

This is responsible for the respiration of the tissues, controlling knowledge, mind and five sense organs and digestion of the food taken in.

2.Keel nokkukaal (Abanan)

It lies below the umbilicus. It is responsible for the downward expulsion of stools and urine, ejaculation of semen and menstruation.

3.Paravukaal (Viyanan)

This is responsible for the motor and sensory function of the entire body and the distribution of nutrients to various tissues.

4.Maelnokkukaal (Uthanan)

It originates at Utharakini. It is responsible for digestion, absorption and distribution of food. It is responsible for all the upward movements.

5.Samaanan (Nadu kaal)

This is responsible for the neutralization of the other 4Valis i.e. Piranan, Abanan, Viyanan and Uthanan. Moreover it is responsible for the nutrients and water balance of the body.

6.Naagan

It is a driving force of eye balls responsible for movements.

7.Koorman

It is responsible for the opening and closing of the eyelids and also vision. It is responsible for yawning.

8.Kirukaran

It is responsible for the salivation of the tongue and also nasal secretion.
Responsible for cough and sneezing and induces hunger.

9.Devathathan

This aggravates the emotional disturbances like anger, lust, frustration etc. As emotional disturbances influence to a great extent the physiological activities, it is responsible for the emotional upsets.

10.Dhanancheyan

Expelled three days after the death by bursting out of the cranium. It is responsible for edema, plethora and abnormal swelling in the body in the pathological state.

As per yugi vaithiya cindhamani

"என்னவே வாதமது எண்பதாகும்

ஏற்றமாம் பேருடைய வெழிலைக் கேளாய்

.....

ஊனுதிரவாதசுரோணிந்தா தானோடு

.....வேதத்தினுண்மை தானே"

AETIOLOGY OF VADHA DISEASES:

According to yugi vaithya cindhamani

"என்னவே வாதம்தா ணென்பதாகும்

இகத்திலே மனிதர்களுக்கு கெய்யுமாறு

பின்னவே பெண்தனையே சோரைஞ் செய்து

பெரியோர்கள் பிராமணரை தூறணித்தும்

வன்னவேவச்சொத்திற் சோரஞ் செய்து

மாதாபிதா குருவைம றந்தபேர்க்கும்

கன்னவே வேதத்தை நிந்தை செய்தால்

காயத்திற் கலந்திடுமே வாதந்தானே"

"தானென்ற கசப்போடுதுவர்ப்பு றைப்பு

சாதகமாய் மிஞ்சுகிலுந் சமைத்த வண்ண

ஆனென்ற வாறினது பொசித்தாலும்

ஆகாயத் தேறலது குடித்தலாலும்

பானென்றபகலுறக்க மிராவிழிப்பு

பட்டினிய மிகவுறுதல் பாரமெய்தல்

சீக்கிரமாய் வாதமது செனிக்குந்தானே"

- Excessive sexual indulgence
- Over consumption of bitters, astringents and rancid foods.
- Drinking rain water
- Day time sleep
- Night time work
- Starvation
- Lifting over weight
- Will initiate and aggravate vali

As per Konganavar Vadha Kaviyam

"ஆச்சப்பா யிதன்கூறை நலதாய்ச்சொன்னோம்

ஆகாகா யிந்நூல்தான் காவியகாண்டத்தில்

வாச்சப்பா வாதத்தின் கூறைச்சொன்னோம்

வாதமதின் வாயுனிலை மயங்கிப்போகும்

காச்சப்பா கலங்கியது தியங்கிப்போகும்

கண்மணியே வதுக்குமத்திபந்தான் கேளு

மாச்சப்பா மக்கினிதான் மதுவோடொக்க

மார்க்கமதாய் கூடிவிளை யாடும்பாரே"

வாதம் தோன்றுதல்:

"வெய்யிலில் நடக்கை யாலும் மிகதண்ணீர் குடிக்கை யாலும்

பையவே உண்கை யாலும் பாகற்காய் தின்கை யாலும்

தையலே வாத ரோகஞ் சனிக்குமென்றறிந்து கொள்ளே"

- Excessive exposure to the sun
- Excessive intake of water
- Postponed of proper intake of food
- Excessive intake of bitter gourd

According to Agathiyar Kanma Kaandam

"நூலென்ற வாதம் வந்த வகை தானேது

நுண்மையாய்க் கன்மத்தின் வகையை கேளு

காலிலே தோன்றியது கடுப்ப தேது

கைகாலிலே முடக்கியது வீக்கமது

கோலிலே படுக்கின்றவிருட்சமான

குழந்தை மரந்தனை வெட்டி மேல்தோ சீவல்

நானிலே சீவசெந்து கால் முறித்தல் நலித்தல் காணே"

- cutting trees and barks
- Breaking the legs of living animals
- cutting the leaves of living trees

According to Agathiyar Gunavagadam,

"அம்புவியில் வாதனோய் வருகும் நேர்மை

அப்பனே சொல்லி கிறேன்றி வாய்க்கேளு

அறுகுமடா மாமிசத்தின் வியாதி யாலும்

அப்பனே சூதகத்தின் பெருக்காலும்

குடிகெடுத்த வாதமது உண்டா மப்பா"

- Muscular diseases
- Menorrhagia
- Consumption of improper preparation of metallic compounds like mercury and lead will cause vadha diseases

CHARACTERISTIC FEATURES OF VATHA DISEASE:

1.As per Theraiyar Vaagadam:

"வாதவீறு அன்னமிறங்காது கடுப்புண்டாம் வண்ணமுண்டாம்

மோது கட்டுரோகம் கரமுண்டா மிருமலுமா முறங்கா தென்றும்

ஓது சூரிய வாதமனலாகு நடுக்கமுண்டாம் பொருள்களாய்த்

தீதெனவே நரம்பிசித்து சந்துகள்தோறும் கடுக்குந் தின்முந்தானே"

- Loss of appetite
- Pain and redness
- Fever and cough
- Insomnia
- Shivering
- Hyperpyrexia

"சந்திரவாத முடம்பு குளிர்த்தெழுந்தே நடுக்குங் சீதவாய்வாம்

முந்திய குத்திவாஞ் சந்துகள் தோறுங் குடைந்து மொளிகள் வீங்கும்

வந்திய தொந்தவாதம் நரம்புகளெல்லா மிசித்துவலம் வீடாது

அந்து அவ்வாகு வாதம் வீக்கமுண்டா முடற்றிமி ருண்டாமே"

- Chillness of the body
- Rigor and spasm
- Pain and tenderness of joints
- Swelling of the joints.

"அறியதிம் மூன்றின தாண்மை சொன்னார் னநந்தி

பறியென நொந்து மற்பச்சை புண்ணாகும்"

-திருமூலர் நாயனார் சிகிச்சா ரத்ன தீபம்

- Pain in the upper and lower limbs, pain in the costochondral junctions will be seen in vadham diseases.

"வாதம் வந்துற்றபோது வயறது பொருமி கொள்ளும்

.....வந்த வாதத்தின் குணமிதாபமே"

-யூகி முனிவர் பெருனூல் வைத்திய காவியம்(1000)

- When vadham increases it produce abdominal discomfort, pain in the hip joint and all the joints of upper and lower limbs, constipation and painful voiding of urine and stools will be seen.
- The diseases will be precipitated in months from aani to karthigai.. i.e.,from June to December,(muthuvenil, kaar and koothirkaalam)

"பகரவே வாதமது கோபித் தப்போ

பண்பாக பெண் போகமது தாமன் செய்யில்

.....கனைக் காலும் கடுப்பு உண்டாமே

- **யூகி வைத்திய சிந்தாமணி பாடல்-285**

- Indulging in sexual act during vitiation of vadham
- Walking for long distance
- Exposing to cold and dampness and harmful combinations like fruits vegetables and tubers with curd causes toxic factors which affects bones and joints

In Aaviyalikkum Amutha murai Surukkam

"சொல்லவே வாதமது மீறிற்றானால்

சொர்வடைந்து வாயுவால் தேகமெங்கும்

மெல்லவே கைகால்களசதி யுண்டாம்

மெய் முடங்கும் நிமிர வெண்ணா திமிருண்டாகும்

வெல்லவே வுடல் பொருமும் வயிருளைக்கும்

விரும்பி யன்னஞ்செல்லாது விந்துநட்டம்

சொல்லவே நாப்புளிக்கும் கழிச்சல் உண்டாகும்

கூறினார் மலையமுனி கூறினாரே"

- Fatigue, tiredness
- Nausea
- Loss of appetite
- Pricking sensation all over the body
- Pain all over the joints.
- Diarrhoea
- Azoospermia
- Incontinence of urine
- Difficulty in flexion and extension
- Constipation

Agathiyar 2000

"வாதத்தின் குணமேதன்னில் மயக்குந்தியங்கும் மலர்சிவக்கும்

பாதங்குளிர்ந்து சருவாங்கம்பற்றி நடக்குமுகங் கடுக்குஞ்

சீதத்துடனே வயிறு புண்ணாஞ் சிரிப்பித் தகுந்தெறி மூச்சாம்

போதத் தண்ணீர்தான் வாங்கும்புகழும் பஞ்சகுணமே"

- Giddiness
- Redness of eyes
- Stabbing pain in the face
- Abdominal distension
- Joint pain in upper and lower limbs
- Numbness in the limbs

- Oliguria
- Drowsiness
- Chillness of the body

வாத மிகுதலின் இயல்பு

“தக்க வாயு கோபித்தால் சந்து வுளைந்து தலைநோவா

மிக்க மூரி கொட்டாவி விட்டங் கெரியு மலங்கட்டும்

ஒக்க நரம்பு தான்முடங்கும் முலர்ந்துவாய்நீ ரூறிவரும்

மிக்க குளிரும் நடுக்கமுமாம் மேனி குன்றி வருங்காணே”

- Pain in the joints
- Head ache
- Excessive yawning
- Constipation
- Burning sensation of the body
- Paralysis
- Excessive salivation
- Chillness and tremor

In kaaviyanaadi

“காணப்பா வாதமீறில் கால்கைகல் பெருத்து நோகும்”

UTHIRAVADHA SURONITHAM

"UTHIRAVADHA SURONITHAM" is one among the eighty types of vadha diseases described by the great siddha pathologist yugi munivar in the textbook of **"YUGI VAIDHYA CHINDHAMANI".**

A form of arthritis of rheumatic origin marked by severe pain and the formation of inflammatory nodules in the region of the joints and especially in the limbs of the body.

According to kathirai velpillai tamil mozhi agarathi

சுரோணிதம் - உதிரம்

உதிரவாதம்

According to sambasivam pillai dictionary

சுரோணிதம் – உதிரம்

மகளிர் சூதகம்

சுரோணித வாதம்:

A disorder of menstruation in women marked by affection in the chest and limbs extreme sensibility to pain, dryness in the dendrites nervous shock, accompanied by intense body pain.

Therayar vaagadam:

"சுரோணிதவாத பிரவிடையான் போதே தொடுக்குந் துடர்ந்து

நோகுங்.....

(பிரிவிடை- பெண்ணின்மத்திய புருவம்)

The disease **"*suronithavatham*"** is occurs in the middle aged women.

"உரைபெறு உதிரவாத சுரோணித முறைக்குங் காலை

தரைபெறு வாதந்தூற்றே சுரோணிதக் குணமுந்தக்க

விரிவுறு பலித்துவாத சுரோணிதக் குணமுமிக்க

சுரைபெறு உதிரவாத சுரோணித குணமுமுண்டாம்"

Vitiation of *vatha* aggravates the signs and symptoms of "vatha suronitham".

Jeeva raksha mirtham classifies this disease into two types,

- Pitha sonitha vatha rogam, which is soft and cause emaciation.
- Slethuma sonitha vatha rogam has polyarthralgia and spindle shaped swelling in the phalanges.

Siddha pathology:

"காணப்பா வாத மீறில் கால்கைகள் பொருத்து நோகும்.....

சொல்லவே வாதமது மீறிற் றானால்

சோர்வடைந்து வாயுவினால் தேமெங்கும்

மெல்லவே கைகால் களசிக லுண்டாகும்

....திமிருண்டாகும்"

- அகத்தியர்

"வளிவாக நாலாயிரத்து நானூற்று நாற்பத்தெட்டு

வந்தணுகில் தேகமதில் வலுவியாதி"

-அகத்தியர்

"எரியநல் வாத மெறிக்குங்வ குணங்கேளு

குறியெனக் கைகால் குளச்சு விலாச் சந்து"

--நோய் நாடல் நோய் முதல் நாடல் திரட்டு

Naadi pathology:

“திருந்துமாம் வாதத் தோடே தீங்கொடு பித்தஜ்சேரில்

பொருத்துகள் தோறும் நொந்து”

-குணவாகடம் நோயின் சாரம்

AETIOLOGY OF SURONITHA VADHAM

“கொண்டிடிற் சரீரம் கலந்தும் பதார்த்தங்கள் கொள்கையாலு

முண்டியிரத்தந் தன்னை யுறிஞ்சிடும் பதார்தத்தாலும்

மிண்டிய சாக்கிரத்தில் விருந்தத் திரைகளாலும்

மண்டுமை துணங்களாலும் வாதள பத்தையாலும்

ஆகிய செல்வமிஞ்சி நடவாம லிருக்கையாலும்

பாகமாங் குதிரையானை பலப்பட வேறலாலும்

பேதமாம் வாயுண்டாய் விபரீதமா யிரத்தஞ்

சோகமாய்வாங்கிச் சோர்ந்து சுரோணித வாதமுண்டாம்”

- Intake of spicy food stuff
- Intake of astringents
- Daytime sleep
- Sedentary life
- Food which decrease the absorption of iron
- Foods which increases the body heat.
- Riding over the elephant and horse

All these factors will affect vatha which along with blood produces Suronithavadham.

According to para rasa sekaram:

“தொழில் பெறுகைப்புக் கார்த்தல் துவர்த்தல் விஞ்சுகினுஞ் சோறும்

பழையதாம் வரகு மற்றையப்பைந்தினை யருந்தினாலும்

எழில் பெறப்பகலுறங்கி இரவினி லுறங்காத தாலும்

மழைநீர் குழலினாலே வாதங் கோபிக்குங்கானே"

1.Over conception of bitters, astringents, savouries and rancid foods

2.Intake of cold water

3.Intake of varagu, thinai

"காணவே மிகவுண்டாலுங் கருதுபட்டினி விட்டாலும்

மானனை யார்கண் மோகமறக்கினு மிகுந்திட்டாலும்

ஏற்பெறு தனது நெஞ்சின் மிகத்துக்க மடைந்திருந்தாலும்

பாரிய காற்றினாளும்படரினும் வாதங்கானும்"

- Eating of excessive intake of food
- Starvation
- Excessive sexual indulgence
- Sleeping in the day time & not sleeping in the night
- Not taking food at proper time, Decreased intake of sour and ghee diet increase the vadham

"பாரினிற் பயப்பட்டாலும் பலருடன் கோபித்தாலும்

காரெனக் கருகியோடிக் கழுமரத்தினாலும்

ஏற்பெறு தனது நெஞ்சின் மிகத்துக்க மடைந்திருந்தாலும்

பாரிய காற்றினாளும்படரினும் வாதங்காணும்"

- Fear
- Anger
- Worry

In textbook of siddha medicine (sabaa pathy kaiyedu)

"வளிதரு காய்கிழங்குவரைவிலா தயிலல் கோழை

முழுதயிர் போன்மி குக்கு முரையிலா வுண்டி கோடல்

களித்தரு முயக்கம் பெற்றோர் கடிசெயல் கருவியாமல்"

- Intake of vadham containing food stuffs
- Intake of cold items
- Exposure to extreme cold air, rain, and snow
- Hereditary
- Stay in mountain

CLINICAL FEATURES OF UTHIRAVADHA SURONITHAM:

In yugi vaithiya chindhamani

“வைகிதமாய்க் கணைகாலு முழங்கால் தானு
மற்கடஞ் சந்து புறவடியும் வீங்கிச்
செய்கிதமாய் சிறுவிரல்கள் மிகவு நொந்து
சிந்தைதடு மாறியே சலிப்புண்டாகும்
பைகிதமாம் பயித்தியத்தில் வாத மிஞ்சிப்
பாரமா யுற்பவித் தழலுண் டாகும்
உய்கிதமா மசனமது தானும் வேண்டா”

- Swelling of the ankle and knee joints
- Swelling of the foot
- Pain in the fingers and toes
- Confusion
- Fatigue
- Loss of appetite

In Dhanvandhiri vaithiyam

“காணுமே எலி விஷம் போல் கனப்புடன் தடிப்புமாக
பூணுடம் புளையங்குத்தும் சொறி கனப்புந்

தோணிருந் துடிப்புத் தேகங் கிள்ளினாற் சோதியாது

மானில முலையாய் சுரோணித வாதமாமே

கையினிற் கறண்டை தண்ணீர் கட்டுஞ் சதைபோல் வீங்கு

மெய்யினைப்பிளக்கும் வாதம் வியாப்பிக்கும் உடம்பதாக்கு

மையலர் உடல் தம்புக்கும் வாதசுரோணித மிதென்னே"

- Pyrexia and swelling of the body as in rat poison intoxication
- Pain and tenderness
- Twitching of muscles
- Loss of sensation
- Swelling of the wrist and phalanges
- Black and redness of swelling due to vascular failure
- Hyperaemia

சுரோணிதவாதம்:

"ஓடிய சுரோணித வாதமுடல்தனை நெஞ்சுலர்ந்து

தேடிய கால் கைகள் திருமே பிளக்க வொண்ணா

வாடிய மேனிதானும் வறண்டிடும் நாவும் பல்லும்

மூடிறக் கடுத்து நொந்து அளைவுடன் குத்துமுண்டே"

According to Vaithiya Cindhamani by kannusamy

உதிரவாத சுரோணிதம் என்ற நோயில் கனைக்காலும், முழங்காலும், சந்துபுறங்களும் வீங்கி வடிவதுடன் விரல்களில் அதிக நோயுண்டாகும். இன்னும் சிந்தை தடுமாறல், சலிப்பு, ஆகார வெறுப்பு இவையும் பெற்றிருக்கும்

- The disease name suronithavatham is also mentioned in **Aaviyalikkum Amuthamurai Churukkam** as painful and swollen joints.
- **Anubogavaithiya Deva Ragasiyam** also deals with vatha diseases. Instead of "Uthiravaatha suronitham" it is mentioned as "Sonithavatharogam".

- **Jeevarakshamirtham** also deals it as sonithavaatharogam in Vaatharogapadalam and the symptoms are polyarthralgia, swelling, anaemia, spindle shaped swelling in the joints.

In pararaasasekaram

"வீழிபெறு சுரோணி தந்தான் மிகவுடன் மெலிவு மாகித்
வாழ்வுறு கையுங்காலும்வசமின்றி யுழன்று நோவாம்
பாழ்பெறு மணங்கி நாளே பயனுறப் பகர்ந்திட் டோமே"

- Decrease in the haemoglobin level
- Pain in the upper and lower limbs
- Swelling especially in the peripheral joint and deformities
- Morning stiffness present more than 1 hr.

"பக்கமும் மார்பும் கூடப்பற்றியே இழுத்துக் கொண்டு
நெக்கியே மார்பிளைத்து நோதாய் நரம்பிழுத்து
ஒக்கவே சயித்தியங்கள் உயர்ந்துடன் மேலும் காலும்
மிக்குமே உதிரவாதம் என்றிதுவிளம்பலாமே"

"சொர்சீதே வுதிர சுரோணித முழங்கால் தாணும்
பொற்கனை காலுங்ந் சந்தும் புறவடி தாணும் வீங்கி
.....முண்டா முறுநூலிற் சொன்ன தாமே"

- Swelling of the ankle and knee joint
- Swelling of hind foot
- Pain in the distal interphalangeal joint

According to Agathiyar Ayulvedham– 1200

"கைகால் நெற்றித்தலை பிடறி கனத்துநொந்து வுளைவுண்டாம்
மெய்யீன்ரூ பந்தான்கெட்டு வெதும்பி விதனமிக வுண்டாந்

தொய்யச் சுருட்டி முடக்கிவிடஞ் சுரோணிதவாதக் குணமதுவென்

றையா முனிவர்தாளி தனாலறியஸ் சொன்னாரரிவாரே"

- Pain in the upper and lower limbs, forehead and cervical region.
- Restricted joint movements.

DIFFERENTIAL DIAGNOSIS:

Among the 80 types of vatdha diseases mentioned in **"yugi vaithiya cindhamani"** the **"Uthiravadhasuronitham"** is differentiated from the following types of suronitham.

1.வாத சுரோணிதம்:

"அறிந்திட்ட அங்கமெலா மெலிவுமாகி

அசைவான தவ்விடங்கள் வீக்கமாகி

.....

வாதசுரோணிதந் தானும் வகுத்தவாறே"

- Emaciation
- Swelling of joints
- Restriction of movements
- Anorexia
- Excessive salivation
- Discomfort

2.சிலேட்டுமவாத சுரோணிதம்:

"பண்பாக வுடல்குளிர்ந்து வயிறு வீங்கிப்

பதைப்பான விடந்தொட்டாற் போல நோவாந்

.....

நற்சிலேட்ம சுரோணிதமாம் நாடுங் காலே"

- Chillness with abdominal distension
- Severe pain
- Headache

- Bronchitis with dyspnoea
- Giddiness
- Dryness of mouth
- Tachycardia
- Syncope and Hallucination
- Anorexia

3.சித்துவாத சுரோணிதம்:

"வாறான சரீரமெலா நுழைந்தே யூதும்

மாசற்ற தோல்தானுந் திரைந்து போகும்

.....

மிக்கசித்து வாதசுரோ ணிதம தாமே"

- Anasarca
- Reduced haemoglobin level
- Wrinkles
- Neural pain
- Bullous eruption as in palms
- Glossy tongue
- Sialorrhoea
- Exfoliation
- swelling
- Warmness.

4.வைகிதவாத சுரோணிதம்:

"ஆமென்ற வீங்கினதோர் இடத்தில் ரத்த

மழுத்தமாய்த் திரண்டுமே யெங்கும் பாய்ந்து

.....

பாரமாய் வைகிதமாம் வாதந் தானே"

- Swelling with hyperaemia
- Soft on touch
- Cough
- Pyrexia
- Irritability

5.பைத்தியவாத சுரோணிதம்:

"உணர்ச்சியாய்ச் சுரோணிதந்தான் மிகவெ தும்பி

ஊக்கமாய்த் தேகமெங்கு மிகவே நொந்து

.....

பயித்தியவாத சுரோணிதத்தின் பண்பு தானே"

- Hyperaemia
- Tenderness in knee, elbow and smaller joints
- Polyarthralgia
- Pyrexia
- Anaemia

6.**உதரவாத சுரோணிதம்:**

"நாடுமே சுரம்வந்து நடுக்கலுண்டாம்

நாவறண்டு கலை நொந்து உடம்ப ழுந்தி

.....

செயவுதர வாதசுரோ ணிதந்தா னென்னே"

- Fever with rigor
- Dryness of mouth
- Diarrhoea
- Headache
- giddiness

- Excessive thirst
- Loss of appetite
- Pain all over the body

IN SIDDHA - MODE OF PATHOLOGY

- Vadham is said to be phenomenon responsible for the movements of the parts involved in locomotor system, hence it is responsible for the articulation of the joints, tendons and muscles.
- Bone and lower abdomen is considered to be the place for vadham.
- Santhiga kabam is said to be the phenomenon which is responsible for the normal maintenance of synovial fluid.
- Synovial fluid provides nutrition for the articular cartilages, disc, meniscus and thereby avoids friction of the bones and erosion of the bones, it helps the smooth articulation.
- In Uthiravadha suronitham due to factors related to diet, habit, environment etc, adversely influence of vali and azhal mainly in mukkutram.
- The involvement of viyanavayu and abanavayu plays a major role in the manifestations of signs & symptoms. Viyana is responsible for all the motor and sensory functions of the body and the nutrition of tissues.
- Abananvayu is responsible for the assimilation of the nutritional factors from the gastro intestinal tract distribution between various thathus and expulsion of waste product through faeces, urination etc...

AZHAL:

- The azhal is responsible for the healthy maintenance of every tissue of the body and its variation results in inflammatory changes in the bone and other accessory structures like tendons, cartilage and synovial membrane which helps in perfect articulation of joints.

IYAM :

- The deterioration of iya humour leads to structural changes in the bones and the fluids in the joints which are mainly controlled by the factors of santhigam.

- Disturbance in humours it produces different clinical manifestations. They Include,
    - Swelling of the joints,
    - Pain
    - Stiffness
    - Restricted movements of the joints due to disturbed vali.
    - Inflammatory changes of the joints like redness hyperaemia, and warmness due to disturbed azhal and erosion of bone margin, increased synovial fluid due to disturbed iyam.
    - The tridosha phenomenon and the functioning of the joints.

"வளிமிகு வபான வியான வாயுகளதிகரிக்கும்

இளமிகு மலனீர்க் கட்டும் இயம்பிய வபானன் செய்யும்

வளிவிலா வியானன் கீலின்விளங்குறு புழைகபோறும்

ஒளியுறு குற்றமெல்லா மொன்றிலென்று லவச்செய்யும்"

- சபாபதி கையேடு(சித்த மருத்துவம், பக்கம் 603

UYIRTHAATHUKKAL:

These are the fundamentals and essential factors in the composition and constitution of the human body.

- Vaatham(vali)
- Pitham(azhal)
- Kabam(iyyam)

PINIYARI MURAIMAI (DIAGNOSIS):

The methodology of diagnosing in siddha science is very unique and solely based on the clinical acumen of the physician. It is based on the three main principles,

- PORIYAL THERTHAL
- PULANAL THERTHAL
- VINATHAL

1. PORIYAL THERTHAL:

Pori means sense of perception. Poriyaltherthal understands by the five sense organs such as nose, tongue, eyes, skin, and ear.

2. PULANAL THERTHAL:

Pulan means objects of senses. Pulanaltherthal understands by the sense objects.

1. Smell (Manam)
2. Taste (suvai)
3. Vision (oli)
4. Somatic sense (ooru)
5. Sound (oosai)

In both of the above said methods, physician, pori and pulan are used as tools for examine the pori and pulan of the patients.

3. VINATHAL:

Vinathal is the process of obtaining the detailed history of the disease by interrogation the patient. By this gathering the history of disease, complaints, and duration, personal history, family history, clinical features, where an accurate history, is available, a disease can be easily diagnosed ever before clinical examinations carried out. It is the focal point of the "physician –patient" relationship and established the bonding necessary for patient cure. The classified method of clinical examinations is known as **ENVAGAI THERVU,** Siddhars have devolved a unique method of diagnosing the diseases by "ENVAGAI THERVU" eight basic diagnostic parameters namely,

i. Sparism
ii. Naa
iii. Niram
iv. Mozhi
v. Vizhi
vi. Malam
vii. Moothiram
viii. Naadi

NAADI NADAI IN UTHIRA VATHA SURONITHAM:

Naadi diagnosis is the confirmatory diagnosis, Naadi is the inherent seat anchor of energy on which vibration the entire thathus of the body are functioning.

1. Vathakapham

2. Kaphavatham.

வாத கபம்:

"பாங்கான வாதத்தில் சேத்தும நாடி

பரிசித்தாற் திமிர்மேவு முளைச்சலாகுந்

.....

.....வெகு நோய்க்கு முறுதி தானே"

கப வாதம்:

"கண்டாயோ சிலேற்பனத்தில் வாத நாடி

கலந்திடுகில் வயிறு பொருமல் கனத்த வீக்கம்

.....

.....பலவும் வந்து சிக்குந் தானே"

Derangements of vatham in uthiravadhasuronitham: `

Abhanan: Constipation, polyuria, menstrual

Viyanan: Pain and tenderness in the affected joints

Samanan: Affected due to the derangements

Koormam: Extra articular features

Kirukiran: Loss of appetite

Derangements of pitham in uthiravadhasuronitham:

Analagam: Loss of appetite

Ranjagam: Anaemia

Saadhagam: Disturbances in regular activities

Aalosagam: Disturbances in vision

Prasagam: Redness

Disturbances of kabham in uthiravadhasuronitham:

Avalambagam: Dyspnoea (due to anaemia)

Kiledham: Loss of appetite

Sandhigam: Restriction of joint movements

Udalthathukkal:

In uthiravathasuronitham cases,

- Saaram
- Senneer
- Oon
- Kozhuppu
- Enbu
- Moolai

Are the most affected

Gnanendhiriyam:

In uthiravathasuronitham cases,

Mei: Pain and tenderness in the joints

Kan: Disturbances of vision (scleritis)

Kanmendhiriyam:

In uthiravathasuronitham cases,

Kai : Difficulty to use the upper limbs

Kaal: Difficulty to use the lower limb

Eruvai: Constipation in some cases

Karuvai: Irregular menstrual cycle in some cases

PININEEKAM:

Siddha system of medicine is a unique system of medicine in which treatment is given both for the body and mind. Thiruvalluvar in his thirukural under the heading "MARUNDHU" mentions about the diseases and its prevention.

So in Siddha system, treatment is not only for the removal of diseases, but for prevention and improving the body condition-Rejuvenation.

1. **Prevention**
2. **Treatment-curative**
3. **Restoration-promotive**

1. PREVENTION:

It is very much, essential and stressed in all siddha literature. Body and mind should be very clean and free from evil thoughts and deeds.

2. TREATMENT:

A Good physician should know about the derangements of humours and should treat the patients on the basis of altered humours.

Treatment is based on,

To bring the tridosham to normal

To treat the disease according to its symptoms through medicines,

To increase the natural immunity

To normalize the tridosham,

"விரேசனத்தால் வாதம் தாழும்" .

Vadha disease can be brought down by vireasanam(purgation), by giving the laxatives and purgatives according to the patient conditions, Four requisites of successful treatment are explained by **"THIRUVALLUVAR"**

"உற்றவன் தீர்ப்பான் மருந்துழைவச் செல்வானென்
றப்பனாற் கூற்றே மருந்து".

3.RESTORATION:

- Reassurance is given to all the patients for fast recovery
- Not to be anxious
- Not to be depressive
- Avoid exposure to cold
- Avoid excessive workload
- To advice the patients to do asanas regularly

MANEGEMENT OF UTHIRAVADHA SURONITHAM:

The treatment of siddha medicine is aimed at keeping the three humours in equilibrium and maintenance of seven elements. So proper diet, medicine and disciplined regimen of life are advised for the healthy living and to restore equilibrium of humours in diseased condition.

- **INTERNAL MEDICINE:**

  'SAMUTHARA CHOORANAM' - 2 grams with Ghee, twice daily, after food for the period of 48 days

- **EXTERNAL MEDICINE:**

  'VADHA NOIKU VELIPRAYOGHA THAILAM'

- **OTTRADAM (THERAPY)**

3.2. REVIEW OF LITERATURE – MODERN ASPECT

BONE:

Bone is a specialized connective tissue in the human body that serves

(1) locomotion by providing the insertion site of the muscles,

(2) protection of the internal organs and the bone marrow as well, and

(3) metabolic function such as storage and provision of calcium to the body

Two major types of bones exist:

1.Flat bones, which are built by intramembranous ossification, and

2.Long bones, which emerge from endochondral ossification.

Intramembranous bone formation is based on the condensation of mesenchymal stem cells, which directly differentiate into bone-forming osteoblasts.

In contrast, during endochondral ossification of the long bones, the mesenchymal stem cells first differentiate into chondrocytes that will further be replaced by osteoblasts. Long bones consist of the

(1) epiphyses, which are protrusions at the ends of the long bones;

(2) the diaphysis constituting its shaft; and

(3) the metaphysis, which are located between the epiphysis and the diaphysis. The metaphysis is separated from the epiphysis by the growth plate, a proliferative cartilage layer, which is essential for the longitudinal growth of bones.

JOINT:

A **joint**, also called an **articulation**, is any place where adjacent bones or bone and cartilage come together (articulate with each other) to form a connection.

Human joints provide the structures by which bones join with one another and may be classified according to histologic features of the union and range of joint motion.

Joints are classified both **structurally and functionally**.

A. STRUCTURAL CLASSIFICATION OF JOINTS:

The structural classification of joints is based on whether the articulating surfaces of the adjacent bones are directly connected by fibrous connective tissue

or cartilage, or whether the articulating surfaces contact each other within a fluid – filled joint cavity.

1. **FIBROUS JOINT** – is where the adjacent bones are united by fibrous connective tissue.
2. **CARTILAGINOUS JOINT** – the bones joined by hyaline cartilage or fibro cartilage.
3. **SYNOVIAL JOINT** – the articulating surfaces of the bones are not directly connected, but instead come into contact with each other within a joint cavity that is filled with a lubricating fluid. This joint allow for free movement between the bones and are the most common joints of the body.

A. FUNCTIONAL CLASSIFICATION OF JOINTS:

The functional classification of joints is determined by the amount of mobility found between the adjacent bones.

1. **Synovial or Diarthrodial joints** which articulate with **free movement**, have a synovial membrane lining the joint cavity, and contain synovial fluid;
2. **Amphiarthroses**, in which adjacent bones are separated by articular cartilage or a fibrocartilage disk and are bound by firm ligaments permitting **limited motion** (e.g., pubic symphysis, intervertebral disks of vertebral bodies, distal tibiofibular articulation, sacroiliac joint articulation with pelvic bones); and
3. **Synarthroses or Immovable joint**, which are found only in the skull (suture lines), where thin, fibrous tissue separates adjoining cranial plates that interlock to prevent detectable motion before the end of normal growth, yet permit growth in childhood and adolescence.

Joints also can be classified according to the connective tissues present.

1. **Symphyses -** have a fibrocartilaginous disk separating bone ends that are joined by firm ligaments (e.g., symphysis pubis and intervertebral joints).

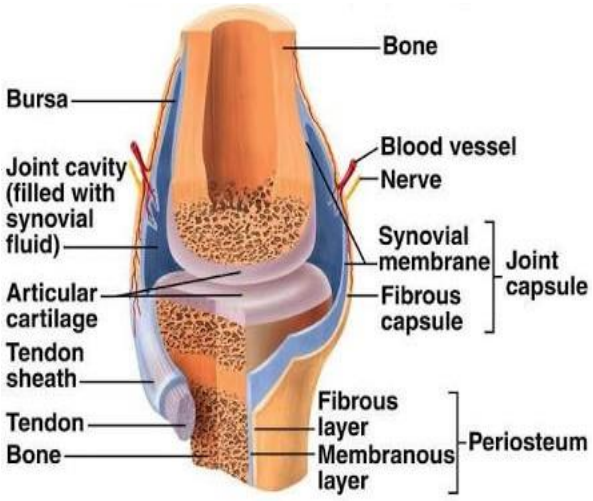
2. **Synchondroses** - the bone ends are covered with articular cartilage, but no synovium or significant joint cavity is present (e.g., sternomanubrial joint).
3. **Syndesmoses** - the bones are joined directly by fibrous ligaments without a cartilaginous interface (the distal tibiofibular articulation is the only joint of this type outside the cranial vault).
4. **Synostoses** - bone bridges are formed between bones, producing ankylosis.

SYNOVIAL JOINT

General Structure

- Synovial(diarthrodial) joints account for most of the body's articulations and are characterized by wide ranges of almost frictionless movement.
- The synovium is a membranous structure that extends from the margins of articular cartilage and lines the capsule of diarthrodial joints, including the temporomandibular joint and the facet joints of vertebral bodies.
- The healthy synovium covers intra-articular tendons and ligaments, as well as fat pads, but not articular cartilage or meniscal tissue.
- Synovium also ensheathes tendons where they pass beneath ligamentous bands and bursas that cover areas of stress such as the patella and the olecranon.

COMPONENTS AND ITS FUNCTION OF SYNOVIAL JOINT:



Structure of synovial joint

1.ARTICULAR CARTILAGE:

The articulating bony surfaces of synovial joints are usually bulbous, sometimes flattened excrescences of cancellous bone, capped by a thin plate of dense cortical bone (the subchondral plate), which is covered by articular cartilage.

- Articular cartilage is a specialized tissue characterized macroscopically by its milky, shelled-almond (hyaline) appearance. It is an **avascular tissue** nourished by diffusion from the vasculature of the subchondral bone and from the synovial fluid.
- Articular cartilage is more than **70% water**, and it is hypocellular compared with other tissues; **chondrocytes** constitute only **1% to 2%** of its total volume.
- Most of the dry weight of cartilage consists of two components:

  1.**Type II collagen** and

  2. the **large aggregating proteoglycan, aggrecan.**

2.CALCIFIED CARTILAGE:

A layer of calcified cartilage exists in the interface between the articular cartilage and its underlying (subchondral) bone.

- The articular cartilage and its calcified cartilage bed are separated from the bone by a wavy, irregular bluish line (on hematoxylin and eosin staining) called the tidemark. The tidemark is similar in appearance and composition to the cement lines in bone and may act as a limit to calcification.
- The collagen in calcified cartilage is **type II** and it is heavily encrusted with **hydroxyapatite**. This
- tissue contains cells that are metabolically active.
- The deep surface of the calcified cartilage merges with the endplate of the underlying bone in an undulating interface.
- This permits a significant increase in **resistance to shearing forces** and helps to keep the cartilage on its bony bed.
- The fibers in the lowermost region are perpendicular to the surface and firmly fixed to the underlying calcified subchondral structures, also positioned to resist shear

3.SUBCHONDRAL BONE:

At the tissue level, the bone located in the subchondral plate and the cancellous bone that supports it are indistinguishable from bone in other sites, the organization of the subchondral bone is specific.

- The subchondral plate on which the calcified cartilage lies is thinner than cortical bone in most sites and contains variable numbers of **mature haversian systems**.
- These systems run parallel to the joint rather than parallel to the long axis of the sheets and interconnecting struts of cancellous bone, which support the plate and fill the epiphyseal end of the bone, differ considerably from joint to joint, but are highly ordered and characteristic for any one joint.
- The major plates are arranged at right angles to the predominating stresses and, together with the subchondral bony plate, are approximately 10 times more deformable than is the cortical bony shaft.
- An increase in this bony structure, so-called subchondral sclerosis, is associated with thickening of the subchondral plate and thinning of the overlying articular cartilage. These changes are pathognomonic of osteoarthrosis and are deleterious to the function of the joint and the health of the overlying articular cartilage

4.SYNOVIAL MEMBRANE:

The synovial membrane serves two functions in the adult joint

1. the provision of nutrients to cells of the articular cartilage and
2. the production of lubricating fluid to ensure the low friction characteristic of joint articulation.

The membrane consists of two distinct layers:

1. the **thin intimal lining or synovial surface layer**, the synovial lining **produces synovial fluid** and represents the direct interface to the intraarticular cavity.
2. the **subintimal layer of connective tissue** that **supports both the lining and the blood vessels** that supply the membrane.

In the normal condition, synovial membrane is an irregular membrane merely two to three cells thick.

In inflammatory disease, this appearance can change dramatically, with both hypertrophy and hyperplasia rapidly developing, resulting in an inflammatory, fibrous membrane.

The main cells of the synovial surface layer and its vascular sublining have been historically divided into two distinctive populations, historically termed

- **synovial type A cells –** have macrophage morphology
- **synovial type B cells –** appears fibroblastic

There is no basement membrane beneath the synovial intima, although both **laminin** and **type IV collagen** may be found underlying the synovial intima. Subintimal tissue is sparsely populated with cells compared with the intima, and fat cells and blood vessels are integrated within this matrix, which is rich in **type I and type III collagen, proteoglycans, and fibronectin**

5.SYNOVIAL FLUID AND JOINT LUBRICATION:

Synovial fluid serves multiple roles in the function of the normal joint. It provides **nutrients to cells** embedded within the cartilage matrix and **lubrication to the articulating surfaces** of the joint. These functions require a surprisingly low amount of fluid, with an average normal volume of 1.1 mL of fluid and a range of 0.13 to 3.5 mL

The composition of synovial fluid is similar to that of plasma, but with additional HA, which provides the high viscosity that is characteristic of synovial fluid. HA, a linear, non-branching polysaccharide, is secreted into the fluid by the fibroblastic cells of the synovial lining and achieves a concentration between 2 and 4 mg/Ml.

In the adult, there is little or no traverse of water through the subchondral plate and only modest flow through the substance of the cartilage, the water displaced by cartilage compression is expressed onto the surface of the cartilage, preferentially peripheral to the zone of impending contact.

The lubrication of synovium on cartilage or synovium upon itself is the result of the affinity of HA for synovial surfaces. Thus, **HA acts as a boundary lubricant for synovium**. This is an important component in the ease of motion of joints, because the periarticular soft tissues contribute much more resistance to joint motion than do cartilaginous surfaces.

In addition, **HA** appears to exert a major influence in **maintaining the volume of synovial fluid** in the joint. HA acts to reduce the volumetric loss that would be expected to occur as fluid pressure increases during joint flexion. As pressure increases, fluid loss is retarded, due to polarized HA accumulation at the interstitial spaces of membrane surface, resulting in elevated osmotic pressure, which retains water molecules within the synovial fluid.

6.CAPSULE:

The joint capsule is vital to the function of synovial joints. It seals the joint space, provides passive stability by limiting movements, provide active stability via its proprioceptive nerve endings and may form articular surfaces for the joint.

It is a dense fibrous connective tissue that is attached to the bones via specialized attachment zones and forms a sleeve around the joint.

- **Outer fibrous layer** – made up of white fibrous tissue, called capsular ligament. This holds together articulating bones and supports the synovium.
- **Inner synovial layer** – a highly vascularized layer of connective tissue. It absorbs and secretes synovial fluid, and is responsible for the mediation of nutrient exchange between blood and joint.

7.LIGAMENTS AND TENDONS:

Stability for the joint is provided by the joint capsule, tendons, and ligaments. These structures govern the motion of a joint and distribute the forces that impinge on the joint.

- Ligaments and tendons are classified as dense connective tissue structures and are generally alike in both structure and function. **Ligaments form connections between bones, whereas tendons provide the attachment of muscle to bone.**
- Ligaments consist of collagen fibrils embedded in a proteoglycan matrix sparsely populated with fibroblastic cells. The microfibril may be considered the basic building block of the ligament derived from the properties of the type I collagen molecule.
- The insertion of ligaments into bone can be classified as direct or indirect. Indirect insertions are more common and are characterized by Sharply fibers, which are

oblique anchor points for the deep fibers within bone. Superficial fibers form a contiguous merger directly with the periosteum in indirect attachment.

- **Ligaments may be viewed as resistant to force, whereas tendons actively transfer force**, but they exhibit the same basic structure.
- Tendons contain a higher ratio of collagen to proteoglycan matrix than ligaments, and the longitudinal alignment of the collagen fibrils is more polarized in tendons. This reflects the variations in directional loading that impinge on ligaments, as opposed to the unidirectional forces that typically are carried by tendons.

8.BURSAE:

A bursa is a small sac lined by synovial membrane filled with synovial fluid. They are placed at key points of friction in a joint, providing the joint with free movement.

They can become inflamed following infection or irritation by over use of the joint(bursitis). Examples of this friction points are where tendons run over the joints, as they do in the knee, a common location for bursitis.

9.MUSCLES:

The muscles surrounding synovial joints are responsible for moving the body in space. These muscle actions are often paired, like flexion and extension or abduction and adduction or pronation and supination or elevation and depression.

10.MENISCI:

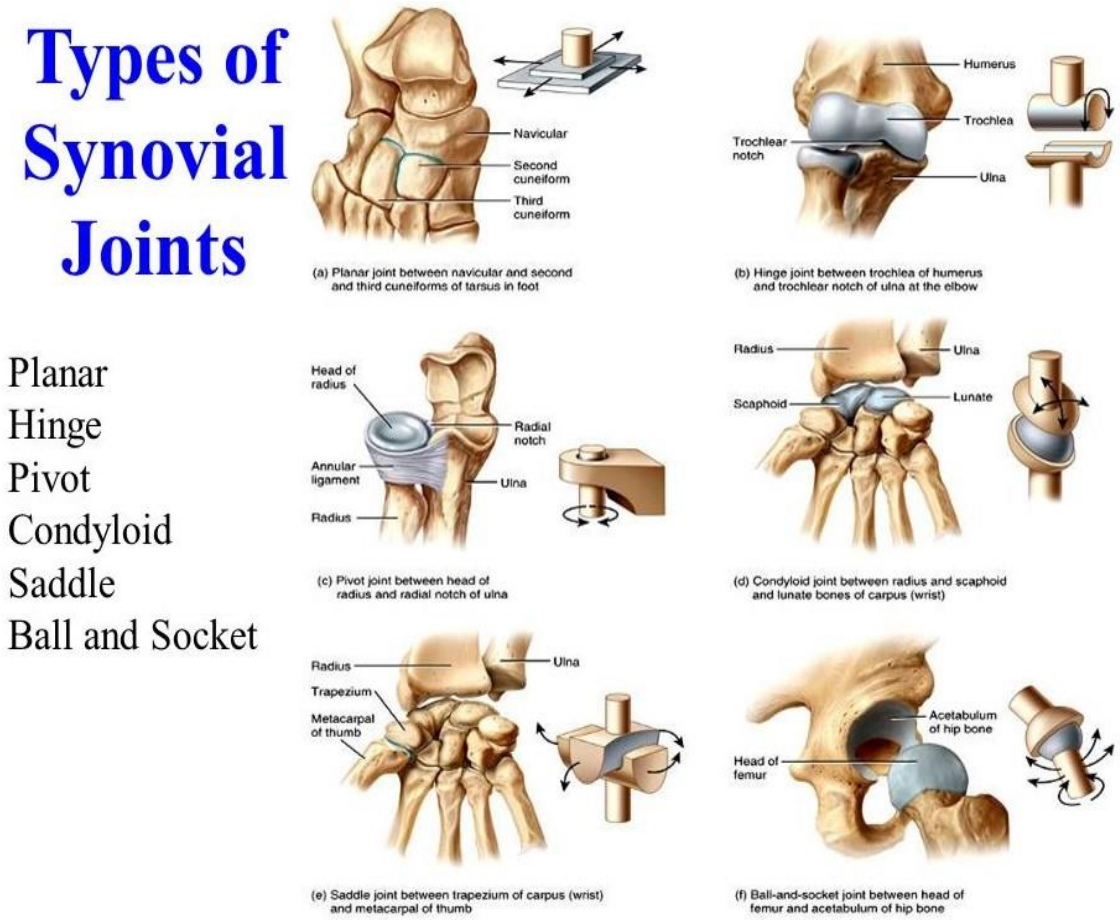
The menisci, like articular cartilages, are for the most part, **avascular**, but at the site of bony attachment, they usually display a surprisingly rich vascular arcade. No nerves or lymphatics have been identified in meniscal tissues. They presumably derive some of their nutrition from synovial fluid, but also by diffusion from vascular plexuses, which are present adjacent to their attachment to bone or fibrous capsule

The fibrocartilage of the meniscus has a biochemical composition considerably different from that of articular cartilage. The water content ranges between 70% and 78%. Inorganic ash accounts for approximately 3% of the wet weight. The remainder of the material, the organic solids, are principally collagen, with type I. Collagen accounts for

60% to 90% of the organic solids. Elastin is present in low concentration (<1%). Proteoglycans constitute less than 10% of the dry weight, and the constituent **glycosaminoglycans** are principally **chondroitin sulfates and dermatan sulfate, with keratin sulfate** representing only a minor component.

Meniscal collagen fibers are arranged circumferentially, presumably to **withstand the tensile hoop stresses generated during load bearing.**

TYPES OF SYNOVIAL JOINTS:



- **PIVOT JOINT** – found in the first few cervical vertebrae, which must twist and turn to allow for rotation of the head and neck.
- **HINGE JOINT** – seen in elbow and knee which are only allowed to bend in one direction.

- **SADDLE JOINT** – which exist between the bones of the fingers and palm, allow the fingers and bones in the hand to rotate in a variety of directions.
- **PLANE JOINT** – allow bones to slide past one another.
- **CONDYLOID JOINT** – are found in the wrist, and allow for a complex range of movement that also holds many bones together.
- **BALL AND SOCKET JOINT** – are synovial joints which are found in several places in the body, including shoulders and hips. It can rotate almost freely around the connection it makes with another bone.

SUBINTIMAL VASCULATURE:

- The vascular supply to the synovium is provided by many small vessels and is shared in part by the joint capsule, epiphyseal bone, and other perisynovial structures. Arteriovenous anastomoses communicate freely with the vascular supply to the periosteum and to periarticular bone.
- As large synovial arteries enter the deep layers of the synovium near the capsule, they branch to form microvascular units in the more superficial subsynovial layers.
- Precapillary arterioles probably play a major role in controlling circulation to the lining layer.
- The surface area of the synovial capillary bed is large, and because it runs only a few cell layers deep to the surface, it has a role in trans-synovial exchange of molecules.
- The **intimal lining, however, is devoid of blood vessels.**

SUBINTIMAL LYMPHATICS:

- Lymphatics are present in the superficial, intermediate, and deeper layers of synovial membrane in synovium from normal individuals or patients with osteoarthritis and rheumatoid arthritis joints, although the number in the superficial subintimal layer is low in normal synovium.
- Little difference in the distribution and number is noted between normal and osteoarthritis synovium, which is characterized by lack of villous hypertrophy.

- Lymphatic channels are plentiful, however, in the subintimal layer in the presence of villous edema hypertrophy and chronic inflammation.

SUBINTIMAL NERVE SUPPLY:

- The synovium has a rich network of **sympathetic and sensory nerves**. The former, which are myelinated and detected with the antibody against S-100 protein, terminate close to blood vessels, where they regulate vascular tone.
- Sensory nerves respond to proprioception and pain via large myelinated nerve fibers and via small (<5μm) unmyelinated or myelinated fibers with unmyelinated free nerve ends (nociceptors).
- The latter are immune-reactive in the synovium for neuropeptides, including substance P, calcitonin gene–related peptide, and vasoactive intestinal peptides.

DISEASES OF JOINTS AND THEIR CLASSIFICATIONS:

A.Infective arthritis:

Bacterial, viral and parasite

1.Acute infection:

- Acute pyogenic arthritis
- Acute gonococcal arthritis
- Acute rheumatic arthritis
- Small pox arthritis

2.Chronic infection:

- Non-specific: Pyogenic arthritis
- Specific: Tuberculous arthritis, syphilitic arthritis, gonococcal arthritis
- Parasitic: Guinea worm arthritis

B.Autoimmune arthrosis

- Rheumatoid arthritis
- Juvenile rheumatoid arthritis
- Seronegative spondyloarthropathy
- Ankylosing spondylitis
- Reiter's disease

- Psoriatic arthritis
- Enteropathic arthritis

C.Degenerative arthrosis(orteoarthritis)

- Osteoarthritis
- Cervical spondylosis
- Lumbar spondylosis

D.Neuropathic arthrosis

- Charcot's arthropathy
- Syringomyelia
- Leprosy
- Diabetes mellitus

E.Metabolic arthritis

- Gout
- Pseudo-gout
- Alkaptonuric arthritis

F.Arthritis in system disorders

- Haemophilic arthritis
- Reactive arthritis

G.Miscellaneous conditions

- Villonodular synovitis
- Synovial chondromatosis

IMMUNE SYSTEM:

The human immune system has evolved over millions of years from both invertebrate and vertebrate organisms to develop sophisticated defense mechanisms to protect the host from microbes and their virulence factors.

The normal immune system has **three** key properties

- a highly diverse repertoire of antigen receptors that enables recognition of a nearly infinite range of pathogens;
- immune memory, to mount rapid recall immune responses and
- immunologic tolerance, to avoid immune damage to normal self-tissues.

A.INNATE IMMUNE SYSTEM:

- From invertebrates, humans have inherited the innate immune system, an ancient defense system that uses germ line-encoded proteins to recognize pathogens.
- Cells of the innate immune system, such as **macrophages, dendritic cells, and natural killer (NK) lymphocytes**, recognize **pathogen-associated molecular patterns (PAMPs)** that are highly conserved among many microbes and use a diverse set of **pattern recognition receptor molecules (PRRs)**.
- Important components of the recognition of microbes by the innate immune system include

  (1) recognition by germ line–encoded host molecules,

  (2) recognition of key microbe virulence factors but not recognition of self-molecules,

  (3) non-recognition of benign foreign molecules or microbes.
- Upon contact with pathogens, macrophages and NK cells may kill pathogens directly or, in concert with dendritic cells, may activate a series of events that both slow the infection and recruit the more recently evolved arm of the human immune system, the adaptive immune system.

B.ADAPTIVE IMMUNE SYSTEM:

- Adaptive immunity is found only in vertebrates and is based on the generation of antigen receptors on **T and B lymphocytes** by gene rearrangements, such that individual T or B cells express unique antigen receptors on their surface capable of specifically recognizing diverse antigens of the myriad infectious agents in the environment.
- Coupled with finely tuned specific recognition mechanisms that maintain tolerance (non-reactivity) to self-antigens, T and B lymphocytes bring both specificity and immune memory to vertebrate host defenses.

THE MAJOR HISTOCOMPATIBILITY COMPLEX:

- The human major histocompatibility complex (MHC), commonly called the **human leukocyte antigen (HLA) complex**, is a 4-megabase (Mb) region on

chromosome 6 (6p21.3) that is densely packed with expressed genes. The best known of these genes are the **HLA class I and class II genes**, whose products are critical for immunologic specificity and transplantation histocompatibility, and they play a major role in susceptibility to a number of autoimmune diseases.

- Many other genes in the HLA region are also essential to the innate and antigen-specific functioning of the immune system. The HLA region shows extensive conservation with the MHC of other mammals in terms of genomic organization, gene sequence, and protein structure and function.

A.Class I Structure:

- MHC class I molecules provide a cell-surface display of peptides derived from intracellular proteins, and they also provide the signal for self-recognition by NK cells.
- Surface-expressed class I molecules consist of an **MHC-encoded 44-kD glycoprotein heavy chain, a non-MHC-encoded 12-kD light chain β2-microglobulin, and an antigenic peptide**, typically 8–11 amino acids in length and derived from intracellularly produced protein.
- The heavy chain displays a prominent peptide-binding groove.
- In HLA-A and –B molecules, the groove is ~3 nm in length by 1.2 nm in maximum width (30 Å × 12 Å), whereas it is apparently somewhat wider in HLA-C.
- Antigenic peptides are non-covalently bound in an extended conformation within the peptide-binding groove, with both N- and C-terminal ends anchored in pockets within the groove (A and F pockets, respectively) and, in many cases, with a prominent kink, or arch, approximately one-third of the way from the N-terminus that elevates the peptide main chain off the floor of the groove.

B.Class II Structure:

- A specialized functional architecture similar to that of the class I molecules can be seen in the example of a class II molecule depicted in with an antigen-binding cleft arrayed above a supporting scaffold that extends the cleft toward the external cellular environment.

- However, in contrast to the HLA class I molecular structure, β2-microglobulin is not associated with class II molecules. Rather, the class II molecule is a heterodimer, composed of a **29-kD α chain and a 34-kD β chain**.
- The amino-terminal domains of each chain form the antigen-binding elements that, like the class I molecule, cradle a bound peptide in a groove bounded by extended α-helical loops, one encoded by the A (α chain) gene and one by the B (β chain) gene.
- Like the class I groove, the class II antigen-binding groove is punctuated by pockets that contact the side chains of amino acid residues of the bound peptide, but unlike the class I groove, it is open at both ends. Therefore, peptides bound by class II molecules vary greatly in length, since both the N- and C-terminal ends of the peptides can extend through the open ends of this groove.

FUNCTIONS OF CLASS I AND CLASS II MOLECULES:

- Class I and class II molecules display a distinctive structural architecture, which contains specialized functional domains responsible for the unique genetic and immunologic properties of the HLA complex. The principal known function of both class I and class II HLA molecules is to bind antigenic peptides in order to present antigen to an appropriate T cell.
- The ability of a particular peptide to satisfactorily bind to an individual HLA molecule is a direct function of the molecular fit between the amino acid residues on the peptide with respect to the amino acid residues of the HLA molecule.
- The bound peptide forms a tertiary structure called the *MHC-peptide complex*, which communicates with T lymphocytes through binding to the TCR molecule.
- The first site of TCR-MHC-peptide interaction in the life of a T cell occurs in the thymus, where self-peptides are presented to developing thymocytes by MHC molecules expressed on thymic epithelium 51 and hematopoietically derived antigen-presenting cells, which are primarily responsible for positive and negative selection, respectively. Thus, the population of MHC–T cell complexes expressed in the thymus shapes the TCR repertoire.

- **Mature T cells** encounter MHC molecules in the periphery both in **the maintenance of tolerance and in the initiation of immune responses.**
- The MHC-peptide-TCR interaction is the central event in the initiation of most antigen-specific immune responses, since it is the structural determinant of the specificity.
- For potentially immunogenetic peptides, the ability of a given peptide to be generated and bound by an HLA molecule is a primary feature of whether or not an immune response to that peptide can be generated, and the repertoire of peptides that a particular individual's HLA molecules can bind exerts a major influence over the specificity of that individual's immune response.

AUTOIMMUNITY:

- The immune system is the capacity to mount an inflammatory response to non-self while avoiding harm to self tissues. The essential feature of an autoimmune disease is that tissue injury is caused by the immunologic reaction of the organism against its own tissues. Autoimmunity, on the other hand, refers merely to the presence of antibodies or T lymphocytes that react with self-antigens and does not necessarily imply that the self-reactivity has pathogenic consequences.
- Autoimmunity is present in all individuals; however, autoimmune disease represents the end result of the breakdown of one or more of the basic mechanisms regulating immune tolerance.
- Currently, three general processes are thought to be involved in the maintenance of selective unresponsiveness to autoantigens.

  (1) sequestration of self-antigens, rendering them inaccessible to the immune system;

  (2) specific unresponsiveness (tolerance or anergy) of relevant T or B cells; and

  (3) limitation of potential reactivity by regulatory mechanisms.

  Derangements of these normal processes may predispose to the development of autoimmunity.

MECHANISM OF AUTOIMMUNITY:

I. Exogenous

A. Molecular mimicry

B. Superantigenic stimulation

C. Microbial adjuvanticity

II. Endogenous

A. Altered antigen presentation

1. Loss of immunologic privilege

2. Presentation of novel or cryptic epitopes (epitope spreading)

3. Alteration of self-antigen

4. Enhanced function of antigen-presenting cells

a. Co-stimulatory molecule expression

b. Cytokine production

B. Increased T cell help

1. Cytokine production

2. Co-stimulatory molecules

C. Increased B cell function

D. Apoptotic defects

E. Cytokine imbalance

F. Altered immunoregulation

AUTOIMMUNE DISEASES:

Organ Specific

1.Graves' disease

2.Hashimoto's thyroiditis

3.Autoimmune polyglandular Syndrome

4.Type 1 diabetes mellitus

5.Insulin-resistant diabetes mellitus

6.Immune-mediated infertility

12.Vitiligo

13.Autoimmune hemolytic anemia

14.Autoimmune thrombocytopenic purpura

15.Pernicious anemia

16.Myasthenia gravis

17.Multiple sclerosis

7.Addison's disease
8.Pemphigus vulgaris
9.Pemphigus foliaceus
10.Dermatitis herpetiformis
11.Autoimmune alopecia
18.Guillain-Barré syndrome
19.Stiff-person syndrome
20.Acute rheumatic fever
21.Sympathetic ophthalmia
22.Goodpasture's syndrome

Organ Nonspecific (Systemic)

1.Systemic lupus erythematosus
2.Rheumatoid arthritis
3.Systemic necrotizing vasculitis
4.Granulomatosis with polyangiitis (Wegener's)
5.Antiphospholipid syndrome
6.Sjögren's syndrome

RHEUMATOID ARTHRITIS:

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis and often results in joint damage and physical disability.

Because it is a systemic disease, RA may result in a variety of extra-articular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities.

The identification and characterization of RF as an autoantibody that binds to the Fc portion of **IgG** was the first direct evidence that autoimmunity might play a role in RA.

Although **IgG and IgM RFs** are the most abundant in RA, IgE RF has also been demonstrated, especially in patients with extra-articular manifestations.

EPIDEMIOLOGY:

- RA affects approximately **0.5–1%** of the **adult population worldwide**. There is evidence that the overall incidence of RA has been decreasing in recent decades, whereas the prevalence has remained the same because individuals with RA are living longer.
- The incidence and prevalence of RA varies based on geographic location, both globally and among certain ethnic groups within a country. For example, the **Native**

American Yakima, Pima, and Chippewa tribes of North America have reported prevalence rates in some studies of nearly **7%.**

- In contrast, many population studies from **Africa and Asia** show lower prevalence rates for RA in the range of **0.2–0.4%.**
- Like many other autoimmune diseases, RA occurs more commonly in **females than in males**, with a **2–3:1** ratio.
- Interestingly, studies of RA from some of the Latin American and African countries show an even greater predominance of disease in females compared to males, with ratios of **6–8:1**. Given this preponderance of females, various theories have been proposed to explain the possible role of **estrogen** in disease pathogenesis.
- Most of the theories center on the role of estrogens in enhancing the immune response. For example, some experimental studies have shown that estrogen can stimulate production of tumor necrosis factor α **(TNF-α)**, a major cytokine in the pathogenesis of RA.

ETIOLOGY:

Although the etiology of RA remains **unknown**, a variety of studies suggest that the interaction of **environmental and genetic factors is responsible**; either one is necessary but not sufficient for full expression of the disease.

A.ROLE OF HLA-DR:

I. HLA-DRB1:

The alleles known to confer the greatest risk of RA are located within the major histocompatibility complex (MHC). It has been estimated that one-third of the genetic risk for RA resides within this locus.

This risk is associated with allelic variation in the **HLA-DRB1** gene, which encodes the **MHC II β-chain molecule**. The disease-associated HLA-DRB1 alleles share an amino acid sequence at positions 70–74 in the third hypervariable regions of the HLA-DR β-chain, termed the **shared epitope (SE)**.

Carriership of the SE alleles is associated with production of **anti-CCP antibodies** and worse disease outcomes. Some of these HLA-DRB1 alleles bestow a high risk of disease, whereas others confer a more moderate risk.

II. HLA-DR4:

The structure of class II MHC molecules on **antigen presenting cells** is associated with increased susceptibility and severity of RA and accounts for about 40% of the genetic influence.

HLA-DR4 occurred in 70% of RA patients, compared with about 30% of controls, giving a relative risk of having RA to those with HLA-DR4 of approximately 4 to 5.

The shared epitope might not be an independent risk factor for RA but instead the presence of the **shared epitope and ACPAs** together is associated with even greater disease severity.

B.ADDITIONAL POLYMORPHISMS:

I.CYTOKINES:

The importance of cytokines in RA is not surprising that many studies have focused on these genes. The most intriguing evidence relates to **tumor necrosis factor (TNF)**. This proinflammatory factor is a major cytokine in the pathogenesis of RA, and the TNF genes are located in the MHC locus on chromosome 6 in humans.

II.CITRULLINATING ENZYME (PADI):

Among the many non-cytokine and non-MHC genetic linkages described for RA, the ones associated with **peptidyl arginase deiminase (PADI) and PTPN22** have the strongest effect on susceptibility.

The PADI genes are responsible for the post-translational modification of **arginine to citrulline**. Four isoforms have been identified, known as **PADI1 through PADI4**.

An extended haplotype in the PADI4 gene that can lead to increased levels of PADI4 protein due to enhanced messenger RNA (mRNA) stability. So, a **twofold increase in risk of RA** was observed with **PADI4 SNPs**

III.PTPN22:

Protein tyrosine phosphatase-22 (PTPN22) associations have been discovered in large-scale screening efforts to identify SNP associations in RA.

C.ENVIRONMENTAL FACTORS:

I.Infectious Agent	**Potential Pathogenic Mechanisms**
Mycoplasma	Direct synovial infection; superantigens
Parvovirus B19	Direct synovial infection
Retroviruses	Direct synovial infection
Enteric bacteria	Molecular mimicry (QKRAA, e.g., in bacterial heat shock proteins)
Mycobacterium	Molecular mimicry (proteoglycans, QKRAA), Immunostimulatory DNA (Toll-like receptor 9 activation)
Epstein-Barr virus	Molecular mimicry (QKRAA in gp110)
Bacterial cell walls	Toll-like receptor 2 activation

II.Smoking

III.Gender

Female predominance – a. Role of oestrogen

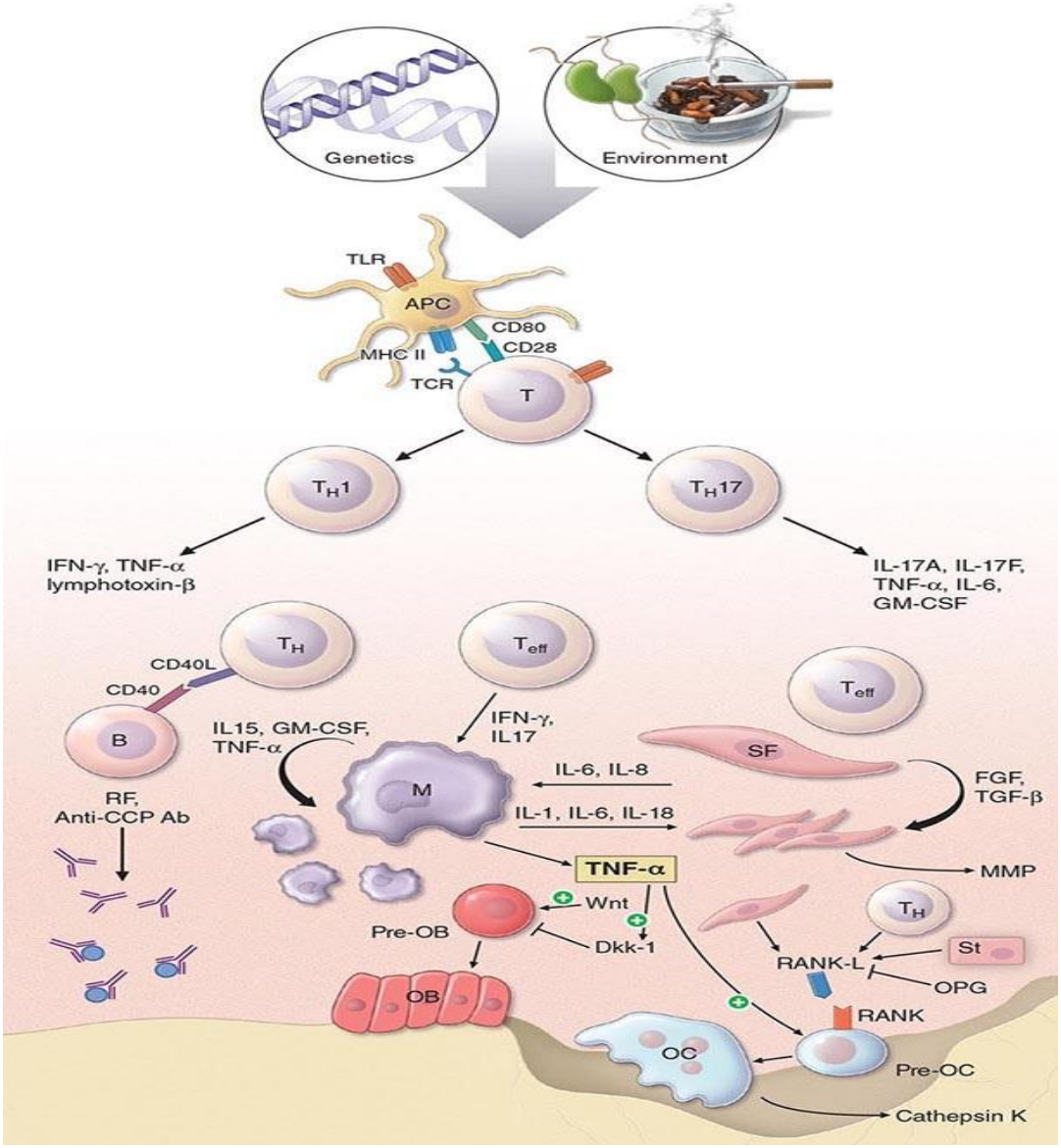
b. During pregnancy

PATHOGENIC MECHANISMS IN RA:

A.AUTOIMMUNITY:

1.Rheumatoid Factor

- The identification and characterization of RF as an autoantibody that binds to the Fc portion of IgG was the first direct evidence that autoimmunity might play a role in RA. For many years, immune complexes comprising RF and other immunoglobulins were thought to play a primary role in the pathogenesis of synovitis



TCR- T cell receptor, T_H-T helper cell, IFN-Interferon, TNF-Tumour Necrosis Factor, IL-Interleukin, TGF-Transforming Growth Factor, FGF-Fibroblast Growth Factor, SF-Synovial Fibroblast, OC-Osteoclast, OB-Osteoblast, RANK-Receptor Activator Of Nuclear Factor, OPG-Osteoprotegerin, TLR-Toll like receptor

2.Anti-citrullinated Protein Antibodies (ACPAs):

- One of the most striking recent observations related to autoantibodies is the observation that immunoglobulins that bind to citrullinated proteins are produced by patients with RA.

- The discovery of antibodies directed against keratin were detected in rheumatoid serum and that the primary target antigen was filament-aggregating protein, **filaggrin**. These antibodies actually bind to epitopes on filaggrin that contain **citrulline,** which is derived from posttranslational **modification of arginine by PADI**. Humans have four isoforms of PADI.
- **PADI2 and PADI4** are especially abundant in **synovium**. The function of PADIs in normal immune responses is not certain; citrullination of some chemokines can decrease activity, and modification of histones can regulate gene expression in stressed cells.
- Induction of PADI expression and citrullination of peptides are not specific to RA and can occur in many inflammatory settings. Not only are other inflammatory arthropathies marked by citrullinated proteins, but other organs such as the **lungs in smokers** have significant PADI activity.
- The presence of CPs in the lungs of smokers could provide the systemic antigen exposure that can contribute to **anti-CP antibody production** and begin the long road to developing RA.

B.INFECTIOUS AGENTS: Direct Infection and Innate Immune Responses

1.Toll-like Receptors and the Inflammasome in the Joint

- Some arthrotropic microorganisms could potentially infect the synovium and cause a local inflammatory response. There is increasing awareness that the innate immune system could also directly affect the onset and course of synovitis. Pathogen-associated molecular pattern receptors, especially the Toll-like receptors (TLRs), are expressed by sentinel cells in the host that provide a **first line of defense**.
- These receptors recognize preserved structures in bacteria and other infectious agents and permit rapid release of inflammatory mediators, activation of antigen-presenting cells, and enhancement of adaptive immune responses

2.Bacteria, Mycobacteria, Mycoplasma and Their Components:

- Active infection of synovial tissue by pyogenic bacteria is an unlikely cause of RA, and extensive searches for a unique or specific organism in synovial tissue or joint

effusions have been negative. Antibodies to certain organisms such as Proteus are reportedly elevated in the blood of patients with RA, but this could represent an epiphenomenon or a nonspecific B cell activation.

- Most RA and reactive arthritis patients contain **bacterial DNA sequences** in their synovium.The bacteria identified are not unique and generally represent a cross-section of skin and mucosal bacteria including Acinetobacter and Bacillus spp.
- It is possible that the synovium functions as an adjunct to the reticuloendothelial system in arthritis, allowing local macrophages to accumulate circulating bacterial products.

3.Epstein-Barr Virus, dnaJ Proteins and Molecular Mimicry

- Epstein-Barr virus (EBV) is a polyclonal B lymphocyte activator that increases the production of RF, and rheumatoid macrophages and T cells have defective suppression of EBV-induced proliferation of human B cells.
- Rheumatoid patients have higher levels of EBV shedding in throat washings, an increased number of virus-infected B cells in the circulating blood, higher levels of antibodies to normal and citrullinated EBV antigens, and abnormal EBV-specific cytotoxic T cell responsiveness.

4.Mycoplasma:

- Mycoplasma-derived superantigens such as from Mycoplasma arthritis can directly induce T cell–independent cytokine production by macrophages and can exacerbate or trigger arthritis.
- There is also a higher prevalence of antimycoplasma pneumoniae IgG antibodies in RA patients.

C.SMOKING:

- A number of environmental factors clearly contribute to RA susceptibility, although no specific exposure has been identified as the pivotal agent. **Smoking** is the best defined environmental risk factor for **seropositive RA.**
- The reason for its influence on the development of synovitis is not fully defined but could involve the activation of innate immunity and PADI in the airway.

- **Increase in protein citrullination** in smokers(tobacco) and increased ability of **SE-containing HLA-DR molecules** to bind some citrullinated proteins which results in **synovitis(auto-reactivity)**.

D.GENDER

- RA is one of many chronic autoimmune diseases that predominates in women. The ratio of female-to-male patients is 2 : 1 to 3 : 1,
- **Estrogens** hormones modulate immune function, an auto-antibody producing B cells exposed to estradiol are more resistant to apoptosis, suggesting that autoreactive B cell clones might escape tolerance.
- Estrogen receptors are expressed on fibroblast-like synoviocytes (FLS) and increase
- production of metalloproteinases. In macrophage cell lines, estrogen can enhance production of TNF.
- **Pregnancy** is often associated with remission of the disease in the **last trimester**. More than three quarters of pregnant patients with RA improve in the first or second trimester, but 90% of these experience a flare of disease associated with a rise in RF titers in the weeks or months after delivery.

PATHOLOGY:

RA affects the synovial tissue and underlying cartilage and bone.

Synovial membrane:

- The synovial membrane, which covers most articular surfaces, tendon sheaths, and bursae, normally is a thin layer of connective tissue.
- It consists primarily of two cell types.

  1.type A synoviocytes (macrophage-derived) and

  2.type B synoviocytes (fibroblast-derived).
- The synovial fibroblasts are the most abundant and produce the structural components of joints, including **collagen, fibronectin, and laminin**, as well as other extracellular constituents of the synovial matrix.

- The sublining layer consists of blood vessels and a sparse population of mononuclear cells within a loose network of connective tissue.
- Synovial fluid, an ultrafiltrate of blood, diffuses through the subsynovial lining tissue across the synovial membrane and into the joint cavity. Its main constituents are **hyaluronan and lubricin.**

Stages and Its Mechanism in Pathology of RA:

The above etiological factors like gene variations, chronic exposure to infective agents, and certain environmental factors will lead to

1.Synovial inflammation and proliferation,

2.Focal bone erosions and

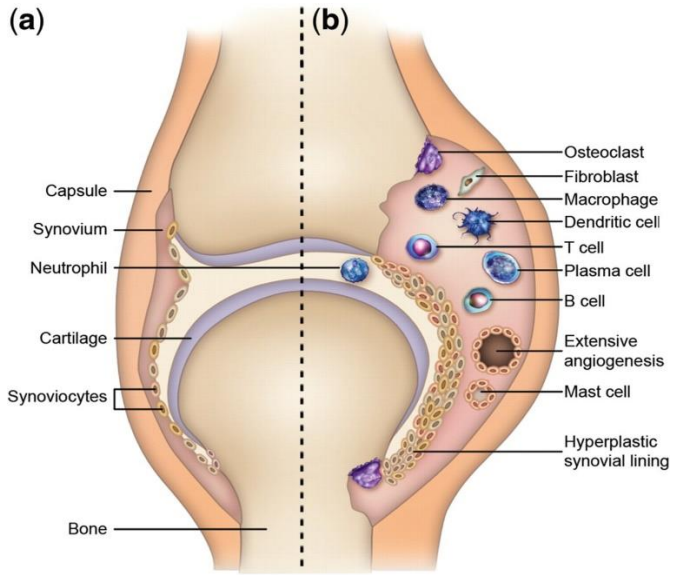
3.Thinning of articular cartilage

1.Synovial inflammation and proliferation:

A.Synovitis::

- Chronic inflammation leads to synovial lining hyperplasia and the formation of pannus, a thickened cellular membrane of granulation–reactive fibrovascular tissue that invades the underlying cartilage and bone.

B.Proliferation and Pannus formation:



a. Normal joint b. Pannus formation in joint

- **Cadherin-11**, the chief organizing molecule of the synovial membrane, confers the invasive nature of the fibroblast-like synoviocytes, the prevailing cell type of the pannus.
- The inflammatory infiltrate is made up of no less than 6 cell types: **T cells, B cells, plasma cells, dendritic cells, mast cells, and a few granulocytes.**
- The T cells comprise 30–50% of the infiltrate, with the other cells accounting for the remainder. The topographical organization of these cells is complex and may vary among individuals with RA.
- The B cells, T cells, and dendritic cells may form higher levels of organization, such as lymphoid follicles and germinal center–like structures.

C.New Vascularisation:

- Growth factors secreted by synovial fibroblasts and macrophages promote the formation of new blood vessels in the synovial sublining that supply the increasing demands for **oxygenation and nutrition** required by the infiltrating leukocytes and expanding synovial tissue.

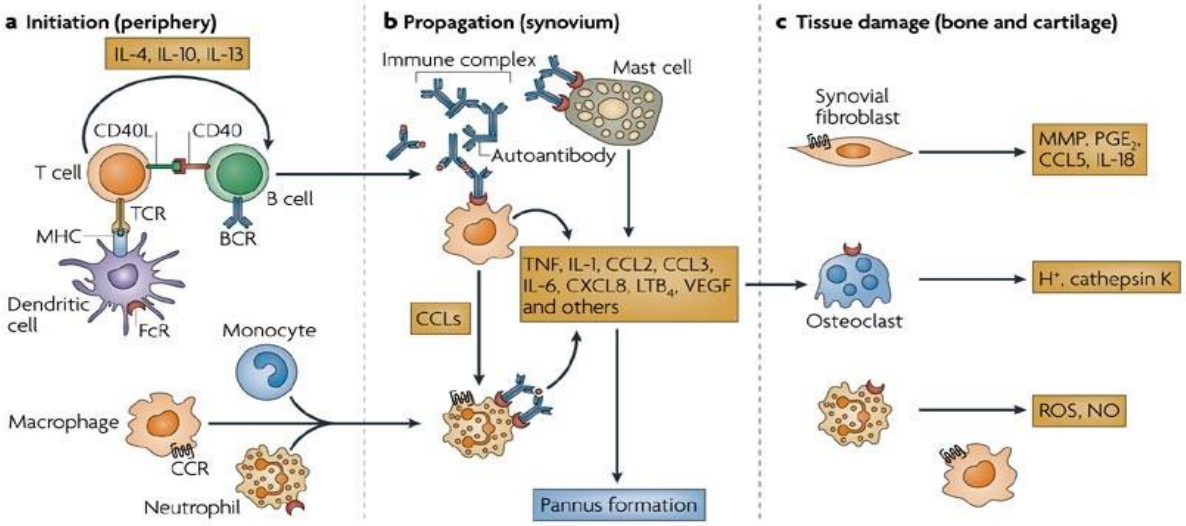
2.Focal bone erosions:

a.1st Stage

- The structural damage to the mineralized cartilage and subchondral bone is mediated by the **osteoclast.**
- Osteoclasts are multinucleated giant cells that can be identified by their expression of **CD68, tartrate-resistant acid phosphatase, cathepsin K, and the calcitonin receptor**. They appear at the pannus-bone interface where they eventually form resorption lacunae.

Common site:

- These lesions typically localize where the synovial membrane inserts into the periosteal surface at the edges of bones close to the rim of articular cartilage and at the attachment sites of ligaments and tendon sheaths.
- This process most likely explains why bone erosions usually develop at the **radial sites of the MCP joints** juxtaposed to the insertion sites of the tendons, collateral ligaments, and synovial membrane.



b.2nd Stage:

- Another form of bone loss is **periarticular osteopenia** that occurs in joints with active inflammation. It is associated with substantial thinning of the bony trabeculae along the metaphysis of bones, and likely results from inflammation of the bone marrow cavity. These bone marrow lesions are often the forerunner of bone erosions.
- The cortical bone layer that separates the bone marrow from the invading pannus is relatively thin and susceptible to penetration by the inflamed synovium.

c.3rd Stage:

- Finally, a third form of bone loss is **generalized osteoporosis**, which results in the thinning of trabecular bone throughout the body.

3.Thinning of articular cartilage:

- Articular cartilage is an **avascular tissue** and was considered to be an inert tissue, but it is now known to be a highly responsive tissue that reacts to inflammatory mediators and mechanical factors, which in turn, alter the balance between cartilage anabolism and catabolism.
- In RA, the initial areas of cartilage degradation are **juxtaposed to the synovial pannus**. The cartilage matrix is characterized by a generalized loss of proteoglycan, most evident in the superficial zones adjacent to the synovial fluid.

- Degradation of cartilage may also take place in the **perichondrocytic zone** and in regions adjacent to the subchondral bone.

At last the extending granular pannus gets organized into fibrous tissue, which bridges the articulating bone ends, leading to **two types of deformity** i.e.,

- **Fibrous ankylosis**
- **Later to Bony ankylosis**

CLINICAL FEATURES:

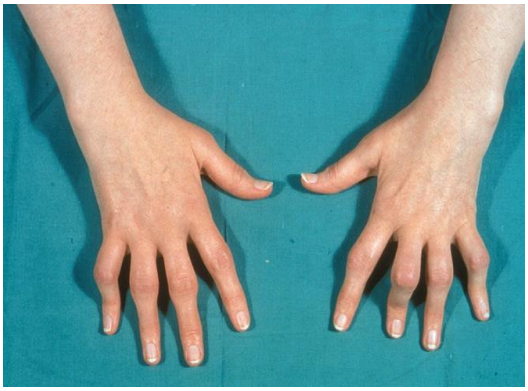
- Edema fluid within inflamed tissues during sleep
- Fatigue, malaise, swollen hands, and diffuse musculoskeletal pain
- Symmetrical Inflammation in Wrists, Metacarpophalangeal (MCP), and Proximal interphalangeal (PIP) joints -most frequently involved joints
- Morning stiffness > 1 hour - cardinal sign of inflammatory arthritis that can appear even before pain and may be related to the accumulation of
- Muscle weakness
- A low-grade fever without chills
- Anorexia.
- Weight loss
- Anaemia
- Depression and anxiety

Distribution of Joints Involved in RA:

Joint Involvement	Percentage (%)
MCP, PIP	91
Wrists	78
Knees	64
Shoulders	65
Ankles	50
Feet	43
Elbows	38
Hips	17

Temporomandibular	8
Spine	4
Sternoclavicular	2
Peri-articular sites	27

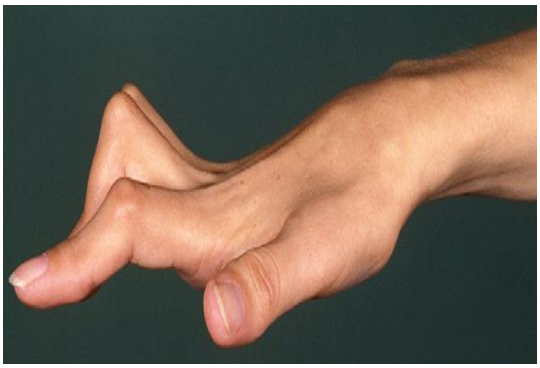
DEFORMITIES OF RA:



Polyarticular arthritis with fusiform swelling of PIP joint

Complete subluxation with ulnar deviation at MCP joint

Swan-neck deformity



Boutonniere deformity

Rupture of Baker's cyst posteriorly at left knee

Rheumatoid nodules in olecranon bursa

Livedo reticularis & Digital gangrene

EXTRA ARTICULAR COMPLICATIONS OF RA:

1.RHEUMATOID NODULES:

- The mature rheumatoid nodule has a central area of necrosis rimmed by a corona of palisading fibroblasts that is surrounded in turn by a collagenous capsule with perivascular collections of chronic inflammatory cells.
- They occur most often on extensor surfaces or pressure points, such as the olecranon process and the proximal ulna, as well as on tendons.
- They are subcutaneous and vary in consistency from a soft, amorphous, entirely mobile mass to a hard, rubbery mass attached firmly to the periosteum.

2.BONE DENSITY:

- Osteopenia
- Osteoporosis

  Which results in Hip fracture, Stress fracture, Vertebral compression fracture

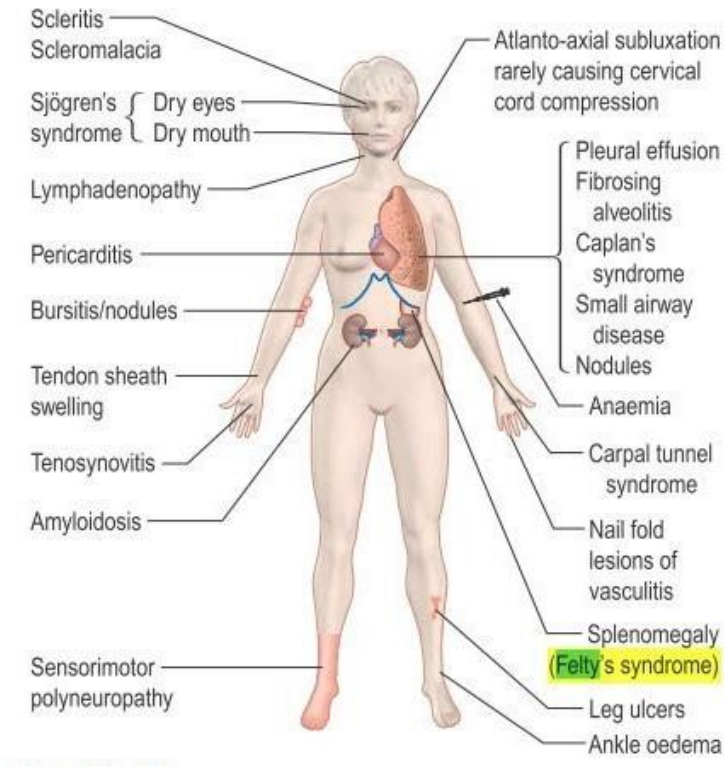
3.MUSCLE:

- Muscle weakness and tenderness
- Muscle atrophy
- Nodular myositis
- Peripheral neuromyopathy
- Steroid myopathy

4.SKIN:

- Rheumatoid nodules

- Senile purpura
- Palmar erythema
- Pyoderma gangrenosum



Extra articular complications of RA

5.EYE:

- Keratoconjuctivitis
- Scleritis
- Episcleritis
- Scleromalacia perforans
- Chronic blepharitis

6.HAEMOTOLOGIC ABNORMALITIES:

- Mild normocytic normochromic anaemia
- Elevated ESR
- Thrombocytosis
- Folate or vitamin B12 deficiency
- Eosinophilia

- Neutropenia

7.VASCULITIS:

- Distal arteritis
- Cutaneous ulceration
- Palpable purpura
- Arteritis of viscera including heart, lungs, bowel, kidney, liver, spleen, pancreas, lymph nodes, or testis

8.RENAL DISEASE:

- AA Amyloidosis
- Renal papillary necrosis
- Membranous nephropathy
- Focal necrotizing glomerulitis

9.PULMONARY DISEASE:

- Pleuritis
- Interstitial pneumonitis
- Pulmonary fibrosis
- Pulmonary nodules
- Caplan's syndrome – pneumoconiosis and RA are synergistic
- Bronchiolitis
- Pulmonary hypertension
- Small airway diseases

10.CARDIOVASCULAR DISEASE:

- Atherosclerosis
- Pericarditis
- Myocarditis
- Endocarditis
- Conduction defects
- Granulomatous aortitis

11.NERVOUS DISORDERS:

- Carpal tunnel syndrome
- Tarsal tunnel syndrome

- Mononeuritis multiplex
- Subluxation of c_1 and c_2 etc…

DIAGNOSIS:

- The clinical diagnosis of RA is largely based on signs and symptoms of a chronic inflammatory arthritis, with laboratory and radiographic results providing important supplemental information.
- In 2010, a collaborative effort between the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) revised the 1987 ACR classification criteria for RA in an effort to improve early diagnosis with the goal of identifying patients who would benefit from early introduction of disease-modifying therapy.

2010 ACR/EULAR Classification

Diagnostic Criteria for Rheumatoid Arthritis

[Cutpoint for RA: ≥6/10])

Joint Involvement	**(0-5)**
1 medium to large joint	0
2-10 medium to large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints (at least one small joint)	5
Serology	**(0-3)**
Negative RF **AND** negative ACPA	0
Low-positive RF **OR** low-positive ACPA	2
High-positive RF **OR** high-positive ACPA	3
Acute Phase Reactants	**1**
Normal CRP **AND** normal ESR	0
Abnormal CRP **OR** abnormal ESR	1

Duration of Symptoms	(0-1)
<6 weeks	0
≥6 weeks	1

DIFFERENTIAL DIAGNOSIS:

Discriminating Features in Patients Presenting with Polyarthritis and Fever

Symptom or Sign	Possible Diagnoses
Temperature >40° C	Still's disease
	Bacterial arthritis
	SLE
Fever preceding arthritis	Viral arthritis
	Lyme disease
	Reactive arthritis
	Still's disease
	Bacterial endocarditis
Migratory arthritis	Rheumatic fever
	Gonococcemia
	Meningococcemia
	Viral arthritis
	SLE
	Acute leukemia
	Whipple's disease
Effusion disproportionately	Tuberculous arthritis
greater than pain	Bacterial endocarditis
	Inflammatory bowel disease
	Giant cell arteritis
	Lyme disease
Pain disproportionately	Rheumatic fever
greater than effusion	Familial Mediterranean fever
	Acute leukemia
	AIDS

Positive test for Rheumatoid Factor	Rheumatoid arthritis
	Viral arthritis
	Tuberculous arthritis
	Bacterial endocarditis
	SLE
	Sarcoidosis
	Systemic vasculitis
Morning stiffness	Rheumatoid arthritis
	Polymyalgia rheumatica
	Still's disease
	Some viral and reactive arthritides
Symmetric small joint synovitis	Rheumatoid arthritis
	SLE
	Viral arthritis
Leukocytosis (>15,000/mm3)	Bacterial arthritis
	Bacterial endocarditis
	Still's disease
	Systemic vasculitis
	Acute leukemia
Leukopenia	SLE
	Viral arthritis
Episodic recurrences	Lyme disease
	Crystal-induced arthritis
	Inflammatory bowel disease
	Whipple's disease
	Mediterranean fever
	Still's disease
	SLE

LABORATORY INVESTIGATIONS:

1.Complete blood count:

- Normocytic hypochromic anaemia
- Eosinophilia
- Thrombocytosis
- Increased ESR
- Neutropenia

2.Increased CRP

3.Increased plasma viscosity

4.Serum proteins

- Decreased albumin
- Increased gammaglobulins
- Increased IgG, IgM, IgA

5. **Serological tests:**

A. IgM (Rheumatoid factor) is detected by the following methods:

I**.Rose Waaler test**: It is more specific and is said to be positive when more than 1:32

II**.Latex test:** It is sensitive and less specific and said to be positive when more than 1:20.

B. Anti-CCP(cyclic citrullinated polypeptide) – Positive test for 95% of RA.

I.ELISA

II.Serum/CMIA

6.**Synovial fluid analysis:**

- Yellow, watery
- Turbidity due to increased WBC from 5000 – 50,000 WBC/ μ^3
- Reduced viscosity
- Increased proteins
- Low sugar content

7.Synovial biopsy and histological examination

8.Arthroscopic examinations to evaluate damage to articular cartilage.

9.Radiological features of RA

Early:

- Soft tissue swelling
- Periarticular osteopenia
- Periosteoitis
- Erosions-periarticular and articular

Later:

- Narrowed joint spaces is caused by loss of cartilage
- Juxta –articular erosion
- Articular surface irregularity
- Subluxation
- Large cystic erosions of bone
- Ankylosis

10.**Ultrasound and MRI** imaging has improved the sensitivity of detecting joint damage earlier in diseases.

- Ultrasound may detect synovitis, effusions, and erosions, in addition to Doppler providing estimates of ongoing inflammation.
- MRI may show inflammatory synovitis that enhances with Gadolinium and shows
  early erosions

11.Arthroscopy- Synovium oedematous, diffusely erythematous, and friable and later the synovium becomes thickened.

12.Computerised tomography

13.Scintigraphy.

TREATMENT AND MANAGEMENT:

1. **DRUGS:**

The amount of clinical disease activity in patients with RA reflects the overall burden of inflammation and is the variable most influencing treatment decisions.

Several developments during the past two decades have changed the therapeutic landscape in RA. They include:

(1) the emergence of methotrexate as the disease- modifying antirheumatic drug (DMARD) of first choice for the treatment of early RA;

(2) the development of novel highly efficacious biologicals that can be used alone or in combination with methotrexate; and

(3) the proven superiority of combination DMARD regimens over methotrexate alone.

The medications used for the treatment of RA may be divided into broad categories:

a. nonsteroidal anti-inflammatory drugs (NSAIDs)
b. glucocorticoids, such as prednisone and methylprednisolone
c. conventional disease-modifying anti-rheumatic drugs (DMARDs) such as hydroxychloroquine, sulfasalazine, methotrexate, and leflunomide
d. biologic DMARDs such as The TNF-inhibitors, Anakinra an IL-1 receptor antagonist, Abatacept, rituximab, and tocilizumab

2. SURGERY:

- Surgical procedures may improve pain and disability in RA—most notably the hands, wrists, and feet, typically after the failure of medical therapy with varying degrees of reported long-term success.
- **Total joint arthroplasty** is an option for advanced joint diseases in larger joints such as the knee, hip, shoulder, or elbow.
- **Silicone implants** are the most common prosthetic for MCP arthroplasty, and are generally implanted in patients with severe decreased arc of motion, marked flexion contractures, MCP joint pain with radiographic abnormalities and severe ulnar drift.
- **Synovectomy** and limited fusion are offered for the early rheumatoid wrist, but they are used much less frequently now compared to the past because of the availability of improved DMARD therapies.
- **Arthrodesis and total wrist arthroplasty** are reserved for patients with severe disease that have substantial pain and functional impairment.

3. PHYSICAL THERAPHY AND ASSISSTIVE DEVICES:

- All patients should receive a prescription for exercise and physical activity.

- Dynamic strength training, community-based comprehensive physical therapy, and physical-activity coaching (emphasizing 30 minutes of moderately intensive activity most days a week) have all been shown **to improve muscle strength and perceived health status**.
- **Foot orthotics** for painful valgus deformity decreases foot pain and resulting disability and functional limitations.
- **Judicious use of wrist splints** can also decrease pain; however, their benefits may be offset by decreased dexterity and a variable effect on grip strength.

4. FOODS:

- Good diet rich in proteins and minerals
- Grains, Olive oil, Fatty fish, Walnuts, Almonds, Flax and Chia seeds which contain rich Omega-3s.
- Berries, Green tea, Grapes, Broccoli, Soy and dietary antioxidants with vitamin A,C,E and Selenium.
- Turmeric, Ginger, Capsaicin have anti-inflammatory properties which can reduce inflammation in the body.

5.SELF-HELP TECHNIQUES:

- Positive mental attitude
- Regular medications
- Regular exercises and Massage
- Adequate sleep
- Modification of daily activities like
  - Using western toilets.
  - Bath aids and railings.
  - Long handle broomstick and mop to clean the floors.
  - Use of walking stick while walking, climbing etc. Avoid walking on hard, rough surfaces.
  - Avoid squatting on the ground for food. Use high chairs and dining table.
  - Avoid squeezing cloths after washing.

REVIEW OF LITERATURE

3.3.DRUG REVIEW – INTERNAL

1 . கடுக்காய்

வேறுபெயர்:

அபையன், அமுதம், அம்ருதா, அரிதகி, வரிக்காய், சாமுதம்

GENERAL PROPERTIES OF KADUKKAI

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Rosids

ORDER: Myrtales

FAMILY: Combretaceae

GENUS: *Terminalia*

SPECIES: *T.chebula*

BOTANICAL NAME: ***Terminalia chebula***

ENGLISH NAME: Chebulic Myrobalan, Ink nut

PART USED:

Unriped fruit and Galls

CHEMICAL CONSTITUENTS:

Gallic acid, Chebupentol, Chebulagic acid, Terminoic acid, p-coumaric acid, Tannin(30-32%), Arjunolic acid

ACTIONS:

Astringent, Alterative, Carminative, Anti septic

Anti – inflammatory, Anti – arthritic, Anti – oxidant

பொதுகுணம்:

"தாடை கழுத்தக்கி தாலு குறியிவிடப்

பீடை சிலிபதமுற் பேதமுட – மாடையெட்டாத்

தூலமிடி புண்வாத சோணிகா மாலையிரண்

டாலமிடி போம்வரிக்கா யால்"

-பதார்த்த குண விளக்கம்- பக்கம் 157

கடுக்காயின் சிறப்பு

"கடுக்காயுந் தாயுங் கருதிலொன்றென் றாலும்

கடுக்காய்த் தாய்க்கதிகங் காண்நீ – கடுக்காய்நோய்

ஓட்டி யுடற்றேற்றும் உற்றவன்னை யோசுவைகள்

ஊட்டியுடற் றேற்று முவந்து"

-அகத்தியர் குணவாகடம்

சுவை : கார்ப்பு

தன்மை: வெப்பம்

பிரிவு: இனிப்பு

வகைகள்:

கருங்கடுக்காய்

செங்கடுக்காய்

வரிக்கடுக்காய்

பால்கடுக்காய்

MEDICINAL USES:

- Fruit kernel paste with water is externally applied for Anti-inflammatory, Analgesic and having purifying and healing capacity of wounds.

- The powdered fruit act as an astringent and is used in haemorrhoids, dentrifice in loose gums, bleeding and ulceration in gums.
- Fruit decoction used in curing diarrhoea and dysentery.
- Fruit powder has Anti-ageing activity.

2. ஓமம்

வேறுபெயர்:

அசமோதம், தீப்பியம்

GENERAL PROPERTIES OF OMAM

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Apiales

FAMILY: Apiaceae

GENUS: *Trachyspermum*

SPECIES: *T.ammi*

BOTANICAL NAME: ***Trachyspermum ammi***

ENGLISH NAME: Bishops weed

PART USED:

Seeds

CHEMICAL CONSTITUENTS:

Essential oil, Thymol, Carvacrol, α and β – pinene, Camphene, Threonine

ACTIONS:

Diuretic, Carminative, Anti – vomiting, Anti – hypertensive, Anti – spasmodic Anti – oxidant, Anti - inflammatory

பொதுகுணம்:

"சீதசுரங் காசஞ் செரியாமந் தம்பொருமல்

பேதியிரைச் சல்கடுப்பு பேராமம் – ஓதிருமல்

பல்லொடுபல் மூலம் பகமிவைநோ யென்செயுமோ?

சொல்லொடுபோம் ஓமமெனச் சொல்"

-அகத்தியர் குணவாகடம்

சுவை: கார்ப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- The seed decoction used in the cases of asthma, anti – dyspnoeic effect, cutaneous disorders, neural and UTI disorders.
- The seed decoction used to enhance the body's resistance.
- The watery extract used to relieve diarrhoea.

3. இஞ்சி

வேறுபெயர்:

அல்லம், ஆர்த்தரகம், ஆத்திரகம், இலாக்கொட்டை, நறுமருப்பு மதில்

GENERAL PROPERTIES OF INJI

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Monocots

SUBCLASS: Commilinids

ORDER: Zingiberales

FAMILY: Zingiberaceae

GENUS: *Zingiber*

SPECIES: *Z. officinale*

BOTANICAL NAME: ***Zingiber officinale***

ENGLISH NAME: Green ginger fresh

PART USED:

Rhizome

CHEMICAL CONSTITUENTS:

Zingiberene, Sesquiterpenes, Curcumene, Gingerols, Gingerdione

ACTIONS:

Carminative, Aphrodisiac, Stimulant

Anti – inflammatory, Immunomodulator, Anti - oxidant

பொதுகுணம்:

"இஞ்சிக் கிழங்குக் கிருமல்ஜயம் ஒக்காளம்

வஞ்சிக்குஞ் சன்னிசுரம் வன்பேதி – விஞ்சுகின்ற

சூலையறும் வாதம்போந் தூண்டாத தீபனமாம்

வேலையுறுங் கண்ணாய் – விளம்பு"

- **பதார்த்த குண விளக்கம் , பக்கம் 70**

சுவை: கார்ப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- Rhizome soaked with honey daily taken at the morning for age preventing and brightness of vision, preventing of skin wrinkling and in albinism and considered as rejuvenating herb.

- It is used in imbalance of vadha and kabha dosha as in rheumatoid and osteoarthritis.
- It helps to relieve weakness of heart, sharp pain due to cardiac condition.
- It is used in congestion of chest, breathing difficulty, severe cough, cold and post-delivery weakness.

4. திப்பிலி

வேறுபெயர்:

கோலகம், கோழையறுக்கி, சௌண்டி, வைதேகி, அம்பு ஆதி மருந்து

GENERAL PROPERTIES OF THIPPILI

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Magnolids

ORDER: Piperales

FAMILY: Piperaceae

GENUS*:* *Piper*

SPECIES*:* *P.longum*

BOTANICAL NAME: ***Piper longum***

ENGLISH NAME: Long pepper

PART USED:

Fruits and roots

CHEMICAL CONSTITUENTS:

Guineensine, Pipernonaline, Pellitorine, Piperine, Pipermonaline, Brachyamide A and B from fruits and Piperlongumine and Sesamine from roots.

ACTIONS:

Analgesic, Carminative, Stimulant

Immunomodulator, Anti – oxidant, Anti - inflammatory

பொதுகுணம்:

"இருமல் குன்மம் இரைப்பு கயப்பிணி

ஈளை பாண்டு சந்யாசம் அரோசகம்

பொருமல் ஊதை சிரப்பிணி மூர்ச்சைநோய்

பூரிக் குஞ்சல தோடம் பீலிகமும்

வரும லப்பெருக் கோடு மகோதரம்

வாதம் ஆதிமுத் தோடஞ் சுரங்குளிர்

பெருமாலைப்புரி மேகப் பிடகமும்

பேருந் திப்பிலிப் பேரங்குரைக்கவே"

- **பதார்த்த குண விளக்கம் , பக்கம் 412**

"ஈளை யிரும லிரைப்புப் பசப்பிணிகள்

மாள வொழியாமல் வாட்டுமே – யாளுமுறை

பாங்கா யறிந்துசெய்வீர் பண்டிதத்தைப் பண்டிதரே

வேங்கைவாய்ப் பாங்கணை மெய்"

- **தேரன் வெண்பா**

சுவை: இனிப்பு

தன்மை: வெப்பம்

பிரிவு: இனிப்பு

MEDICINAL USES:

- It is used to mitigate the diseases due to kabha dosha.
- The fruit powder is used to cure cough, bronchitis, asthma, malarial fever, diarrhoea and jaundice.
- Root and fruit decoction used for treating gonorrhoea, menstrual pain, RTI, TB.
- Root decoction used in sciatica, hemiplegia, arthritis.

5. பெருங்காயம்

வேறுபெயர்:

அத்தியாகிரகம் , இங்கு , காயம் , சந்துநாசம் , பூதநாசம்

GENERAL PROPERTIES OF PERUNGAYAM

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Apiales

FAMILY: Apiaceae

GENUS: *Ferula*

SPECIES: *F.asafoetida*

BOTANICAL NAME: ***Ferula asafoetida***

ENGLISH NAME: Asafoetida

PART USED:

Oleo – gum resin

CHEMICAL CONSTITUENTS:

Disulfides, Tri – and Tetrasulfides, Glucuronic acid, Galactose, Arabinose, Umbelliferone, Foetidin, Coumarin

ACTIONS:

Sedative, Anti – spasmodic, Anthelmintic, Emmenogogue, Expectorant, Carminative

பொதுகுணம்:

"தந்தவே தந்த மூலத்தெழும்பிணி
சருவகாளம் விருச்சிகங்கீடம்மா
மந்தம்வாதம் உதாவர்த்தம் அல்குல்நோய்
மார்பணங்கட்ட குன்மம்மகோதரம்
உந்துகெர்ப்பத்தின் வித்திரஞ்சூலைச்சூர்
உதிரப்பூச்சி சிலேத்துமத்துறும்வலி
வந்தமெய்க்கடுப் போடிவைமுற்றுமே
மாயுநாறுநற் காயங்கிடைக்கினே"

-தேரையர் குணவாகடம்

சுவை: கைப்பு, கரகரப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- It has been used as the remedy for abdominal pain and constipation.
- Resin used in the treatment for nervous disorders and spasmodic disorders.
- In respiratory disorders like whooping cough, bronchitis, asthma – 30 to 60 mg of resin combine with 2 teaspoons of honey, a quarter teaspoon of white onion juice and 1 teaspoon of betel leaf juice- thrice daily would keep the disorders away.
- Asafoetida used in sterility, unwanted abortion, premature labour, excessive menstruation, leucorrhoea.

6. வாய்விடங்கம்

வேறுபெயர்:

வாயுவிளங்கம் , கேரளம் , வாய்விலங்கம் , வர்னனை , வாய்விடங்கம்

GENERAL PROPERTIES OF VAIVIDANGAM

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Ericales

FAMILY: Primulaceae

GENUS: *Embelia*

SPECIES: *E.ribes*

BOTANICAL NAME: ***Embelia ribes***

ENGLISH NAME: False black pepper, White flowered embelia

PART USED:

Fruit, Seeds

CHEMICAL CONSTITUENTS:

Embelin, Quercitol, Tannin, Christembine, Embelic acid and Vilangin

ACTIONS:

Anthelmintic, Carminative, Stomachic, Stimulant

Anti – oxidant, Anti – inflammatory, Analgesic

பொதுகுணம்:

"பாண்டுகுட்டம் குன்மம் பருந்தூல நோய்வாதத்

தீண்டு திரிவிடஞ் சிரந்துண்டம் – பூண்டமடி

நோய்விளங்கக் காட்டாத நுண்கிருமி யாசனப்புண்

வாய்விளங்கங்காட்டா விருமார்"

- **அகத்தியர் குணவாகடம்**

"வாதகுரு வாயுடம்பு வாதமறுத் தப்படியே

வேதையுலோ கங்களிலே வேண்டினாற் – பாத

விரதமுதற் கையாட லென்றா லிசையும்

வர்னனை நீமனத்தில் வை"

- **தேரன் வெண்பா**

சுவை : கைப்பு

தன்மை : வெப்பம்

பிரிவு : கார்ப்பு

MEDICINAL USES:

- To prevent the flatulence, the fruit powder is mixed with milk and given twice a day.
- To prevent worm infestation, the seed powder mixed with honey is given thrice a day. Then next day ask the patient to take 15 ml castor oil. The worms are died and expelled out.
- It is used in the imbalance of vadha dosha and maintains the vadha.
- Externally the seed powder paste is used in the scorpion and snake bite.

7. இந்துப்பு:

வேறுபெயர்:

சைந்தவம் , சிந்தூரம் , சந்திரனுப்பு , மதிகூர்மை , மதியுப்பு , மிந்தாச்சொல்

GENERAL PROPERTIES OF ROCK SALT

CATEGORY: Hallide mineral

FORMULA: Nacl

CRYSTAL SYSTEM: Cubic

CRYSTAL CLASS: Hexoctahedral

IDENIFICATION:

FORMULA MASS: 58.433 g/mol

COLOR: Colorless or White

CRYSTAL HABIT: Predominantly cubes but also Granular, Fibrous and Compact

FRACTURE: Conchoidal

TENACITY: Brittle

LUSTER: Vitreous

STREAK: White

SPECIFIC GRAVITY: 2.17

OPTICAL PROPERTIES: Isotropic

REFRACTIVE INDEX: n=1.544

SOLUBILITY: Water soluble

ACTIONS:

Carminative, Diuretic, Stimulant, Laxative

பொதுகுணம்:

"அட்டகுன்ம மந்தம் அசிர்க்கரஞ்சூர் சீதபித்தந்

துட்டவையம் நாடிப்புண் தோடங்கள் – கெட்டமலக்

கட்டுவிட விந்தையக் காமியநோய் வன்கரப்பான்

விட்டுவிட விந்துப்பை விள்"

"சென்னிக்கண்ணா பற்றூர் செவிகவுள்கண் டம்பகநோய்

சந்நியா சங்காசந் தாகமிரைப் – புன்னிரத்த

மூலஞ் சிலந்திநளி மூடிகநஞ் சூதை வலி

சூலஞ் சிதையுமிந்தாற் சொல் "

- குணபாடம் தாது சீவ வகுப்பு

MEDICINAL USES:

- It is used in the treatment for gastritis, indigestion, dental and genital disorders, venous ulcers.

8. கல்லுப்பு

வேறுபெயர்:

கடற்குருவி

GENERAL PROPERTIES OF KALLUPU:

IUPAC NAME: Sodium chloride

CHEMICAL FORMULA: Nacl

CRYSTAL STRUCTURE: Face – centered, cubic

MOLAR MASS: 58.44 g/mol

APPEARANCE: Colorless crystals

ODOR: Odorless

DENSITY: 2.165 g/cm^3

MELTING POINT: 801℃

SPECIFIC HEAT CAPACITY: 36.79 J/k.mol

GEOMETRY: Octahedral

பொதுகுணம்:

"ஐயமறுஞ் சூலை யரோசிபித்தஞ் சத்தியோடு

வெய்யபிணி யட்டகுன்மம் விட்டேகும் – பெய்வளையே

வாதமதி தாகம் மலக்கட்டும் போமுலகிற்

கோதறுகல் லுப்பைக் கொடு"

- குணபாடம் தாது சீவ வகுப்பு

ACTIONS:

Anti vadha, Anti pitham

MEDICINAL USES:

- It is used to cure vadha dosha, Thirst, Constipation, Vomiting**.**

9. எவட்சாரம் :

வேறுபெயர் :

மர உப்பு

GENERAL PROPERTIES OF YAVACHARAM:

IUPAC NAME: Potassium carbonate

OTHER NAMES: Carbonate of potash, Pearl ash, Salt of tartar, Salt of wormwood

CHEMICAL FORMULA: CK_2O_3

MOLAR MASS: 138.20 g/mol

APPEARANCE: White, hygroscopic solid

DENSITY: 2.43 g/cm^3

MELTING POINT: 891℃

BOILING POINT: Decomposes

SOLUBILITY: Water soluble

பொதுகுணம் :

"குய்யம் களம்நா கொடிறுவா யிவ்விடதோ

யைய மிரைப்பிரும லாசனப்புண் – பைய்யவுறு

கீடவிடஞ் சோபை கிராணியையும் பம்பரம்போ

லாடவிடு மெய்யவட்சா ரம்"

"அட்டகுன்மஞ் சூலை யதிதூல முட்டினத்தா

லொட்டிவரு வாத முதரநோய் – துட்டமந்தம்

நீடுகபம் நீரடைப்பு நீங்காப் பீலிகமிவை

யொடுமெவட் சாரத்தா லுன்”

- குணபாடம் தாது சீவ வகுப்பு

ACTIONS:

Deobstruent, Stimulant, Alterative, Diuretic

MEDICINAL USES:

- It is a mineral supplement used to treat or prevent low amounts of potassium in the blood.
- Potassium helps our cells, kidneys, heart, muscles, nerves work properly.
- It is used in the treatment of ascites, diarrhoea, indigestion, ulcers.

DRUG REVIEW – EXTERNAL MEDICINE

1.ஊமத்தை

வேறுபெயர்:

உம்மத்தை

GENERAL PROPERTIES OF OOMATHAI

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Solanales

FAMILY: Solanaceae

GENUS: *Datura*

SPECIES: *D.metal*

BOTANICAL NAME: ***Datura metal***

ENGLISH NAME: Devils's trumpet, Thorn apple

PART USED:

Leaves, Flower, Fruit, Seeds

CHEMICAL CONSTITUENTS:

Hyoscyamine, Scopolamine, Tricyclic diterpene, Daturabietariene

ACTIONS:

Anodyne, Anti - spasmodic

பொதுகுணம் :

"நாய்க்கடியால் வந்து நலிசெய் விரணமும்போம்

வாய்குழிப்புண் கட்டிகளு மாறுங்காண் – தீக்குணத்தைச்

சேமத்தில் வைத்திலிடந் தீருமுத்தோ டங்களறும்

ஊமத்தை யிங்குணத்தை யுன்னு"

- **அகத்தியர் குணவாகடம்**

சுவை: கைப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- The leaves have been proved to relieve asthma and externally used to relieve swelling and pain in arthritis.
- Powdered seeds mixed with butter are administered internally for impotence.

2. சடாமாஞ்சில்

வேறுபெயர்:

சடமாசி , ஜடமாஞ்சி , பைசாசி , சடிலை , மாமிசி பூதசேசிநி

GENERAL PROPERTIES OF SADAMAANJIL

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Dipsacales

FAMILY: Caprifoliaceae

GENUS: *Nardostachys*

SPECIES: *N.grandiflora*

BOTANICAL NAME: ***Nardostachys grandiflora***

ENGLISH NAME: Spikenard, Muskroot, Valerina root

PART USED:

Root (Rhizome)

CHEMICAL CONSTITUENTS:

Acaciin, Ursolie acid, Kanshone A, Nardosinonediol, Oleonolic acid, β sitosterol

ACTIONS:

Analgesic, Stimulant, Anti - spasmodic

பொதுகுணம் :

"குட்டஞ் சிலந்திவிடம் கோர புராண சுரம்

உட்டினங்கால் பேதிகண்ணோய் ஒட்டிருமல் - சொட்டிரத்த

பித்தமிரைப் பேகும் பெருங்கோரை என்றுரைக்குஞ்

சுத்தசடா மாஞ்சிலை சொல்"

- **அகத்தியர் குணவாகடம்**

சுவை: கார்ப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- The analgesic activity of Sadamanjil oil used to relieve pain and swelling of arthritis and spondylosis.
- It has hepatoprotective characteristics thus useful in hepatitis, prevent enlargement of liver and jaundice.
- It is beneficial for hyperactive children and helpful to reduce hyperactivity, restlessness and aggressiveness.
- It is used to impact black colour to hair and prevents greying of hair.

3.ஓமம்

வேறுபெயர்:

அசமோதம் , தீப்பியம்

GENERAL PROPERTIES OF OMAM

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Apiales

FAMILY: Apiaceae

GENUS: *Trachyspermum*

SPECIES*: T.ammi*

BOTANICAL NAME: ***Trachyspermum ammi***

ENGLISH NAME: Bishops weed

PART USED:

Seeds

CHEMICAL CONSTITUENTS:

Essential oil, Thymol, Carvacrol, α and β – pinene, Camphene, Threonine

ACTIONS:

Diuretic, Carminative, Anti – vomiting, Anti – hypertensive, Anti – spasmodic Anti – oxidant, Anti - inflammatory

பொதுகுணம்:

"சீதசுரங் காசஞ் செரியாமந் தம்பொருமல்

பேதியிரைச் சல்கடுப்பு பேராமம் – ஓதிருமல்

பல்லொடுபல் மூலம் பகமிவைநோ யென்செயுமோ?

சொல்லொடுபோம் ஓமமெனச் சொல்"

-அகத்தியர் குணவாகடம்

சுவை: கார்ப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- The seed decoction used in the cases of asthma, anti – dyspnoeic effect, cutaneous disorders, neural and UTI disorders.
- The seed decoction used to enhance the body's resistance.
- The watery extract used to relieve diarrhoea.

4.சூடம்

வேறுபெயர்:

கருப்பூரம் , சுடர்கொடியோன் , பூரம் , தீபம்

GENERAL PROPERTIES OF CAMPHOR:

- It is waxy, flammable, white or transparent solid with strong aroma.
- It is found in wood of the Camphor laurel (*Cinnamomum camphora*).

IUPAC NAME: 1,7,7 – Trimethylbicyclo heptan- 2- one

OTHER NAME: 2- Bornanone, Bornan – 2 - one

CHEMICAL FORMULA: $C_{10}H_{16}O$

MOLAR MASS: 152.24 $g.mol^{-1}$

APPEARANCE: White, translucent crystals

ODOR: Fragrant and penetrating

DENSITY: 0.992 $g.cm^{-3}$

MELTING POINT: 175-177̊C

BOILING POINT: 209℃

VAPOR PRESSURE: 4 mmHg

ACTIONS:

Anodyne, Stimulant

பொதுகுணம்:

"கிருமிசல தோடங் கிளைவலிப்பு சந்நி

பொருமுமந்தம் அங்கிபட்ட புண்ணோ – டெரிசுரங்கள்

வாந்திபித்தஞ் சீதமுறு வாதஞ் செவிமுகநோய்

காந்திகருப் பூரமொன்றாற் சாற்று"

- குணபாடம் தாது சீவ வகுப்பு

சுவை: விறுவிறுப்புடன் கூடிய கைப்பும் கார்ப்பும்

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

MEDICINAL USES:

- It is readily absorbed through skin, where it selectively stimulates nerve endings sensitive to cold, producing a warm sensation when applied externally.
- It also induces a slight local anesthesia, and has an antimicrobial secondary effect.
- It is used to treat sprains, swelling and inflammation

5.நவாச்சாரம் :

வேறுபெயர்:

இஷ்டிகை , சல்லிகை , சூளிகை , படு

GENERAL PROPERTIES OF NAVACHARAM:

IUPAC NAME: Ammonium chloride

OTHER NAME: Sal ammoniac, Salmiac, Sal armagnac

CHEMICAL FORMULA: ClH_4N

MOLAR MASS: 53.49 $g.mol^{-1}$

APPEARANCE: White Solid, hygroscopic

ODOR: Odorless

DENSITY: 1.5274 g/cm^{-3}

MELTING POINT: 338℃

BOILING POINT: 520℃

VAPOR PRESSURE: 133.3Pa

SOLUBILITY: Soluble in liquid ammonia, alcohol, slightly soluble in acetone

ACIDITY: 9.24

FLASH POINT: Non – flammable

ACTION:

Diaphoretic, Diuretic, Expectorant

பொதுகுணம்:

"குன்மம் குடற்சூலை கொல்லும் மகோதரத்தை

வன்மையுறு கல்லடைப்பை மாற்றுங்காண் – சன்மக்

கவிச்சுமுத் தோடங் கனவாத நீக்கும்

நவாச்சார மாதே நவில்"

- குணபாடம் தாது சீவ வகுப்பு

MEDICINAL USES:

- Navacharam mixed with Hemidesmus indicus root decoction and given twice daily for the treatment of rheumatoid arthritis and dental disorders.
- On external application, it reduces joint pain and swelling.
- It is used in used in the treatment hepato and spleenomegaly, chronic fever.

6. நல்லெண்ணெய்:

வேறுபெயர்:

திலம்

GENERAL PROPERTIES OF GINGELLY OIL:

KINGDOM: Plantae

DIVISION: Angiosperms

CLASS: Eudicots

SUBCLASS: Asterids

ORDER: Lamiales

FAMILY: Pedaliaceae

GENUS*:* *Sesamum*

SPECIES: *S.indicum*

BOTANICAL NAME: ***Sesamum indicum***

ENGLISH NAME: Gingeli oil

PART USED:

Seed oil

CHEMICAL CONSTITUENTS:

Lignans sesamolin, Sesamin, Pinoresinol, Lariciresinol

ACTIONS:

Demulcent, Emollient, Laxative, Nutritive

பொதுகுணம்:

"புத்திநயனக்குளிர்ச்சி பூரிப்பு மெய்ப்புளகஞ்

சத்துவங் கந்தி தனியிளமை – மெத்தவுண்டாங்

கண்ணோய் செவிநோய் கபாலவழல் காசநோய்

புண்ணோய்போ மெண்ணெய்யாற் போற்று”

- அகத்தியர் குணவாகடம்

சுவை : இனிப்பு

தன்மை : வெப்பம்

பிரிவு : இனிப்பு

MEDICINAL USES:

- Calcium, zinc, copper minerals in oil plays an important role in growth of bone, healing, regrowth of bone and prevent osteoporosis.
- Externally it can increase skin elasticity, smoothness and reduce the appearance of age spots.
- It can help to reduce the inflammation and discomfort of various conditions such as gout and arthritis by reducing the swelling of joints.

MATERIALS AND METHODS

4. MATERIALS AND METHODS

SELECTION OF DRUGS:

I had chosen the Siddha Herbal – Mineral formulation drug **"SAMUTHARA CHOORANAM"(Internal)** for this study from classical siddha literature **'Pranarashamirtha Sindhu'** and **"VADHA NOIKU VELIPRAYOGHA THAILAM"(External)** from **'The Pharmacopoeia of siddha research medicines'.**

The raw drugs were purchased from the raw drug shop R.N.RAJAN & CO, Paris. After getting proper authentication from the Head of the Department of Medicinal Botany and Pharmacology(Gunapadam), GSMC, Chennai-106 the medicines were prepared.

4.1.INTERNAL MEDICINE

SAMUTHARA CHOORANAM

INGREDIENTS:

Purified Induppu*(Rock salt)*	***- 5 gms***
Purified Yavacharam *(Potassium carbonate)*	***- 5 gms***
Purified Kaluppu *(Sodium chloride impura)*	***- 5 gms***
Omam*(Trachyspermum ammi)*	***- 20 gms***
Kadukkai*(Terminalia chebula)*	***- 20 gms***
Thippili*(Piper longum)*	***- 20 gms***
Inji*(zingiber officinale)*	***- 20 gms***
Perungayam*(Ferula asafoetida)*	***- 20 gms***
Vaividangam*(Embelia ribes)*	***- 20 gms***

METHOD OF PURIFICATION:

HERBAL DRUGS:

Purified and dried under classical text

MINERAL DRUGS:

INDUPPU:

Soaked in rice vinegar for 3 days, dried in sunlight till all water content gets evaporated and then salt was powdered in stone mortar.

YAVACHARAM:

Dissolved in Goat's urine, filtered, dried in sunlight and then salt was powdered in stone mortar.

KALUPPU:

Soaked in rice vinegar for few seconds. Remove the humidity of kaluppu by placing it in dry cotton cloth and dried in sunlight. At last, salt was powdered in stone mortar

MATERIALS REQUIRED:

4.1.1TERMINALIA CHEBULA



4.1.2. ZINGIBER OFFICINALE



4.1.3. PIPER LONGUM



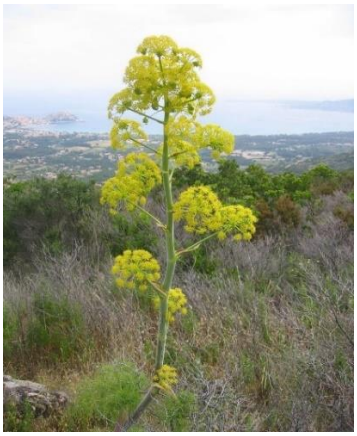
4.1.4. TRACHYSPERMUM AMMI



4.1.5. EMBELIA RIBES



4.1.6. FERULA ASAFOETIDA



4.1.7.INDUPPU (ROCK SALT)

Before purification **After purification**


4.1.8.KALUPPU (SODIUM CHLORIDE IMPURA)

Before purification **After purification**


4.1.9.YAVACHARAM (POTASSIUM CARBONATE)

Before purification **After purification**


4.1.10.SAMUTHARA CHOORANAM

METHOD OF PREPARATION:

Above purified drugs were grinded separately and mixed well together. Then filter them as a fine powder and weighed. Atlast the powder was stored in the air tight container.

DOSAGE : Two gram(twice daily) for 48 days

ADJUVENT : Ghee

INDICATION : Vadham(80), Paandu(5), Moolam(8), Kiragani(11), Kunmam(8), Magotharam(8) , Vayirru valli, Vaayu.

REFERENCE : Pranarashamirtha sindu . Pg.no:166

4.2.EXTERNAL MEDICINE

VADHA NOIKU VELIPRAYOGHA THAILAM

INGREDIENTS:

Oomathai ilai chaaru*(Datura metal)*	- 2.2 L
Omam*(Trachyspermum ammi)*	- 47 gm
Sadamanjil*(Nardostachys grandiflora)*	- 47 gm
Soodam*(Camphor)*	- 23 gm
Purified Navacharam*(Ammoni chloridum)*	– 12 gm
Gingelly oil	- 400 ml

METHOD OF PURIFICATION:

HERBAL DRUGS:

Purified and dried under classical text.

MINERAL DRUG:

NAVACHARAM – Dissolved in cow's urine and filtered. Boiled till all the water content gets evaporated and dried it in sunlight. Then salt was powdered in stone mortar.

MATERIALS REQUIRED:

4.2.1.DATURA METAL

4.2.2.NARDOSTACHYS GRANDIFLORA

4.2.3.TRACHYSPERMUM AMMI

4.2.4.NAVACHARAM (AMMONIUM CHLORIDE)

Before purification

After purification

4.2.5.CAMPHOR

4.2.6.GINGELLY OIL

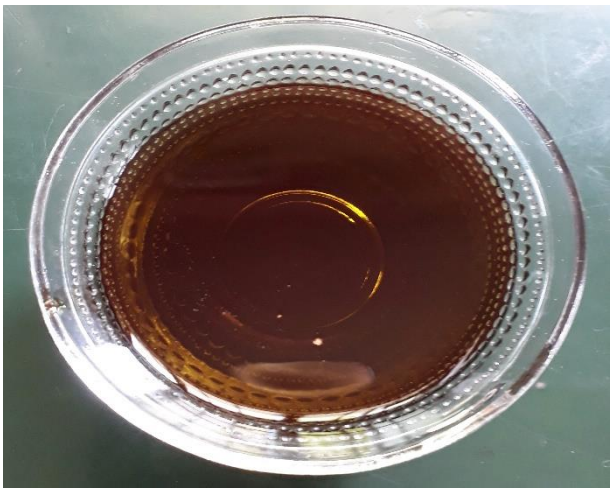
4.2.7.Omam and Sadamanjil were made into decoction and then filtered


4.2.8.Gingelly oil and the filtered decoction were mixed in the vessel and heated


4.2.9.oomathai leaf juice had been mixed with the above oil content and heated


4.2.10.Prepared oil was filtered in the receiver containing purified Navacharam and Camphor

4.2.11. VADHA NOIKU VELIPRAYOGHA THAILAM



METHOD OF PREPARATION(EXTERNAL):

Omam and sadamanjil were added in water and boiled it, made into decoction and then filtered. Oomathai ilai charu, gingelly oil and the prepared decoction were mixed well and heated. Heat it well until needed consistency is attained. Navacharam and camphor powders was placed in the vadikalam. After this camphor and navacharam was well dissolved in the vadikalam (receiver) containing thailam. After the thailam was cooled under room temperature, it was bottled up in the air tight container.

INDICATIONS: All kinds of pain in the joints, muscles, nerves and burses are relieved.

REFERENCE: The pharmacopoeia of siddha research medicines. Pg.no:122

4.3.THERAPY: OTTRADAM

DEFINITION:

The required plant parts, grains and others are put in a container, fried or boiled or heated and then tied in a cloth bag. The bag is put on the affected areas and then gently compressed and released in a rhythemic manner for few minutes or till the heat subsides. It is also called as Otral. Cold paste can also be used as otral.

Bronze, Iron, Rod, Sand, Cloth, Mud vessel are also heated and used for fomentation to give relief from pain.

PROCEDURE:

The turmeric powder and salt was placed in half of the lemon and tied up in a bundle(kizhi). The kizhi was dipped in the heated **vadha noiku veliprayogha thailam**. Then the heated kizhi was used to give ottradam on the affected areas. Repeat the process for seven times.

MEDICINAL USES:

Control the Inflammation of joints, Swelling, Redness, Pain and Improves the Circulation in the affected part.

REFERENCE: Aruvai maruthuvam pg.no:44

4.4. STANDARDIZATION PARAMETERS

4.4.1.ORGANOLEPTIC CHARACTERS:

State:

Solid

Appearance:

Greenish brown in color

Nature:

Mild coarse in nature

Taste:

Astringent with mild Pungent

Odor:

Strong characteristic

4.4.2.PHYSICOCHEMICAL EVALUATION:

Percentage Loss on Drying

10gm of test drug was accurately weighed in evaporating dish. The sample was dried at 105oC for 5 hours and then weighed.

Percentage loss in drying = Loss of weight of sample/Wt of the sample X 100

Determination of Total Ash

3 g of test drug was accurately weighed in silica dish and incinerated at the furnace a temperature 400 ºC until it turns white in color which indicates absence of carbon. Percentage of total ash will be calculated with reference to the weight of air-dried drug.

Total Ash = Weight of Ash/Wt of the Crude drug taken X 100

Determination of Acid Insoluble Ash

The ash obtained by total ash test will be boiled with 25 ml of dilute hydrochloric acid for 6mins. Then the insoluble matter is collected in crucible and will be washed with hot water and ignited to constant weight. Percentage of acid insoluble ash will be calculated with reference to the weight of air-dried ash.

Acid insoluble Ash = Weight of Ash/Wt of the Crude drug taken X 100

Determination of Water Soluble Ash

The ash obtained by total ash test will be boiled with 25 ml of water for 5 mins. The insoluble matter is collected in crucible and will be washed with hot water, and ignite for 15mins at a temperature not exceeding 450ºC. Weight of the insoluble matter will be subtracted from the weight of the ash; the difference in weight represents the water soluble ash. Calculate the percentage of water-soluble ash with reference to the air-dried drug.

Water Soluble Ash = Weight of Ash/Wt of the Crude drug taken X 100

Determination of Alcohol Soluble Extractive

About 5 g of test sample will be macerated with 100 ml of Alcohol in a closed flask for twenty-four hours, shaking frequently during six hours and allowing to stand for eighteen hours. Filter rapidly, taking precautions against loss of solvent, evaporate 25 ml of the filtrate to dryness in a tared flat bottomed shallow dish, and dry at 105ºC, to constant weight and weigh. Calculate the percentage of alcohol-soluble extractive with reference to the air-dried drug.

Alcohol sol extract = Weight of Extract/ Wt of the Sample taken X 100

Determination of Water Soluble Extractive

About 5 g of the test sample will be macerated with 100 ml of chloroform water in a closed flask for twenty-four hours, shaking frequently during six hours and allowing to stand and for eighteen hours. Filter rapidly, taking precautions against loss of solvent, evaporate 25 ml of the filtrate to dryness in a tared flat bottomed shallow dish, and dry at 105ºC, to constant weight and weigh. Calculate the percentage of water-soluble extractive with reference to the air-dried drug.

Water soluble extract = Weight of Extract/ Wt of the Sample taken X 100

Determination of pH

About 5 g of test sample will be dissolved in 25ml of distilled water and filtered the resultant solution is allowed to stand for 30 mins and the subjected to pH evaluation

4.4.3.HEAVY METAL ANALYSIS BY AAS

Standard: Hg, As, Pb and Cd – Sigma

Methodology

Atomic Absorption Spectrometry (AAS) is a very common and reliable technique for detecting metals and metalloids in environmental samples. The total heavy metal content of the sample KN was performed by Atomic Absorption Spectrometry (AAS) Model AA 240 Series. In order to determination the heavy metals such as mercury, arsenic, lead and cadmium concentrations in the test sample.

Sample Digestion

Test sample digested with 1mol/L HCl for determination of arsenic and mercury. Similarly for the determination of lead and cadmium the sample were digested with 1mol/L of HNO3.

Standard reparation

As & Hg- 100 ppm sample in 1mol/L HCl

Cd & Pb- 100 ppm sample in 1mol/L HNO3

4.4.4.TLC AND HPTLC ANALYSIS:

TLC Analysis

Test sample was subjected to thin layer chromatography (TLC) as per conventional one dimensional ascending method using silica gel 60F254, 7X6 cm (Merck) were cut with ordinary household scissors. Plate markings were made with soft pencil. Micro pipette were used to spot the sample for TLC applied sample volume 10-micro liter by using pipette at distance of 1 cm at 5 tracks. In the twin trough chamber with different solvent system Toulene: Ethyl Acetate: Acetic Acid (1.5:1:0.5) After the run plates are dried and was observed using visible light Short-wave UV light 254nm and light long-wave UV light 365 nm

High Performance Thin Layer Chromatography Analysis

HPTLC method is a modern sophisticated and automated separation technique derived from TLC. Pre-coated HPTLC graded plates and auto sampler was used to achieve precision, sensitive, significant separation both qualitatively and quantitatively. High performance thin layer chromatography (HPTLC) is a valuable quality assessment tool for the evaluation of botanical materials efficiently and cost effectively. HPTLC method offers high degree of selectivity, sensitivity and rapidity combined with single-step sample preparation. In addition it is a reliable method for the quantitation of nano grams level of samples. Thus this method can be conveniently adopted for routine quality control analysis. It provides chromatographic fingerprint of phytochemicals which is suitable for confirming the identity and purity of medicinal plant raw materials.

Chromatogram Development

It was carried out in CAMAG Twin Trough chambers. Sample elution was carried out according to the adsorption capability of the component to be analysed. After elution, plates were taken out of the chamber and dried.

Scanning

Plates were scanned under UV at 366nm. The data obtained from scanning were brought into integration through CAMAG software. Chromatographic finger print was developed for the detection of phytoconstituents present in each extract and Rf values were tabulated.

4.4.5.PHYTOCHEMICAL ANALYSIS

Extraction

Sample Extraction were carried out with water and the resulting extract was utilized for the phytochemical analysis

Test for alkaloids:

Mayer's Test: To the test sample, 2ml of mayer's reagent was added, a dull white precipitate revealed the presence of alkaloids.

Test for coumarins:

To the test sample, 1 ml of 10% sodium hydroxide was added. The presence of coumarins is indicated by the formation of yellow color.

Test for saponins:

To the test sample, 5 ml of water was added and the tube was shaken vigorously. Copious lather formation indicates the presence of Saponins.

Test for tannins:

To the test sample, ferric chloride was added, formation of a dark blue or greenish black color showed the presence of tannins.

Test for glycosides- Borntrager's Test

Test drug is hydrolysed with concentrated hydrochloric acid for 2 hours on a water bath, filtered and the hydrolysate is subjected to the following tests. To 2 ml of filtered hydrolysate, 3 ml of choloroform is added and shaken, choloroform layer is separated and 10% ammomia solution is added to it. Pink colour indicates presence of glycosides.

Test for flavonoids:

To the test sample about 5 ml of dilute ammonia solution were been added followed by addition of few drops of conc. Sulfuric acid. Appearance of yellow color indicates the presence of Flavonoids.

Test for phenols:

Lead acetate test: To the test sample; 3 ml of 10% lead acetate solution was added. A bulky white precipitate indicated the presence of phenolic compounds.

Test for steroids:

To the test sample, 2ml of chloroform was added with few drops of conc. Sulphuric acid (3ml), and shaken well. The upper layer in the test tube was turns into red and sulphuric acid layer showed yellow with green fluorescence. It showed the presence of steroids.

Triterpenoids

Liebermann–Burchard test: To the chloroform solution, few drops of acetic anhydride was added then mixed well. 1 ml concentrated sulphuric acid was added from the sides of the test tube, appearance of red ring indicates the presence of triterpenoids.

Test for Cyanins

A. Aanthocyanin:

To the test sample, 1 ml of 2N sodium hydroxide was added and heated for 5 min at 100^{o}C. Formation of bluish green colour indicates the presence of anthocyanin.

Test for Carbohydrates - Benedict's test

To the test sample about 0.5 ml of Benedict's reagent is added. The mixture is heated on a boiling water bath for 2 minutes. A characteristic coloured precipitate indicates the presence of sugar.

Proteins (Biuret Test)

To extracts 1% solution of copper sulphate was added followed by 5% solution of sodium hydroxide, formation of violet purple colour indicates the presence of proteins.

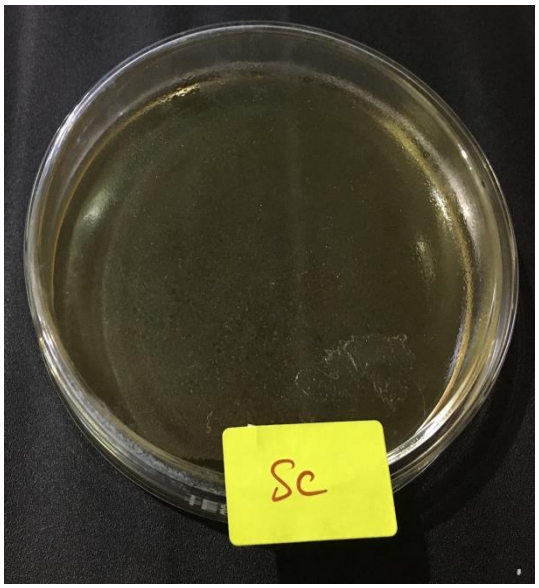
4.4.6. STERILITY TEST BY POUR PLATE METHOD:

Objective

The pour plate techniques were adopted to determine the sterility of the product. Contaminated / un sterile sample (formulation) when come in contact with the nutrition rich medium it promotes the growth of the organism and after stipulated period of incubation the growth of the organism was identified by characteristic pattern of colonies. The colonies are referred to as Colony Forming Units (CFUs).

Methodology

About 1ml of the test sample was inoculated in sterile petri dish to which about 15 mL of molten agar 45oC were added. Agar and sample were mixed thoroughly by tilting and swirling the dish. Agar was allowed to completely gel without disturbing it. (about 10 minutes). Plates were then inverted and incubated at 37o C for 24-48 hours. Grown colonies of organism was then counted and calculated for CFU.



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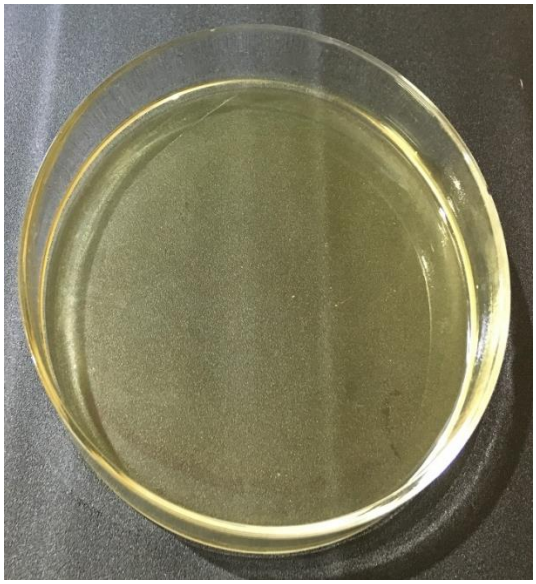


Observation

No growth was observed after incubation period. Reveals the absence of specific pathogen

4.5. TOXICOLOGICAL STUDY

4.5.1. ACUTE ORAL TOXICITY STUDY OF *SAMUTHARA CHOORANAM* (OECD GUIDELINE – 423)

Introduction:

- The acute toxic class method is a stepwise procedure with the use of 3 animals of a single sex per step.
- Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgement on the acute toxicity of the test substance.
- This procedure is reproducible, uses very few animals and is able to rank substances in a similar manner to the other acute toxicity testing methods.
- The acute toxic class method is based on biometric evaluations with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment.

- In principle, the method is not intended to allow the calculation of a precise LD50, but does allow for the determination of defined exposure ranges where lethality is expected since death of a proportion of the animals is still the major endpoint of this test.
- The method allows for the determination of an LD50 value only when at least two doses result in mortality higher than 0% and lower than 100%.
- The use of a selection of pre-defined doses, regardless of test substance, with classification explicitly tied to number of animals observed in different states improves the opportunity for laboratory to laboratory reporting consistency and repeatability.

Principle of the Test:

It is the principle of the test that based on a stepwise procedure with the use of a minimum number of animals per step, sufficient information is obtained on the acute toxicity of the test substance to enable its classification. The substance is administered orally to a group of experimental animals at one of the defined doses. The substance is tested using a stepwise procedure, each step using three animals of a single sex. Absence or presence of compound-related mortality of the animals dosed at one step will determine the next step, i.e.

− no further testing is needed

− dosing of three additional animals, with the same dose

− dosing of three additional animals at the next higher or the next lower dose level.

The method will enable a judgment with respect to classifying the test substance to one of a series of toxicity classes.

Methodology:

Selection of Animal Species

The preferred rodent species is the wistar albino rat, although other rodent species may be used. Healthy young adult animals are commonly used laboratory strains should be employed. Females should be nulliparous and non-pregnant. Each animal, at the commencement of its dosing, should be between 6 to 8 weeks old and the weight (150-200gm) should fall in an interval within±20 % of the mean weight of any previously dosed animals.

Housing and Feeding Conditions

The temperature in the experimental animal room should be 22ºC + 3ºC. Although the relative humidity should be at least 30% and preferably not exceed 70% other than during room cleaning the aim should be 50-60%. Lighting should be artificial, the sequence being 12 hours light, 12 hours dark. For feeding, conventional laboratory diets may be used with an unlimited supply of drinking water. Animals may be group-caged by dose, but the number of animals per cage must not interfere with clear observations of each animal.

Preparation of animals:

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions.

Test Animals and Test Conditions:

Sexually mature Female Wistar albino rats (150-200gm) were obtained from TANUVAS,Madhavaram, Chennai. All the animals were kept under standard environmental condition (22±3°C). The animals had free access to water and standard pellet diet (Sai meera foods, Bangalore).

Preparation for Acute Toxicity Studies

Rats were deprived of food overnight (but not water 16-18 h) prior to administration of the, ***Samuthara chooranam***.

The principles of laboratory animal care were followed and the Institutional Animal Ethical Committee approved the use of the animals and the study design

IAEC approved Number: 1248/AC/09/CPCSEA-9/DEC-2013/12

Test Substance	: **SAMUTHARA CHOORANAM**
Animal Source	:TANUVAS,Madhavaram, Chennai.
Animals	: Wister Albino Rats (Female-3+3)
Age	**:** 6-8 weeks
Body Weight on Day 0	**:** 150-200gm.
Acclimatization	**:** Seven days prior to dosing.

Veterinary examination	**:** Prior and at the end of the acclimatization period.
Identification of animals	**:** By cage number, animal number and individual marking by using Picric acid.
Number of animals	: 3 Female/group,
Route of administration	: Oral
Diet	**:** Pellet feed supplied by Sai meera foods Pvt Ltd, Bangalore
Water	**:** Aqua guard portable water in polypropylene bottles.
Housing & Environment	**:** The animals were housed in Polypropylene cages provided with bedding of husk.
Housing temperature	**:** between 22ºC $\pm$ 3ºC.
Relative humidity	**:** between 30% and 70%,
Air changes	**:** 10 to 15 per hour and
Dark and light cycle	**:** 12**:**12 hours.
Duration of the study	**:** 14 Days

Administration of Doses:

Samuthara chooranam was suspended in water and administered to the groups of wistar albino rats in a single oral dose by gavage using a feeding needle. The control group received an equal volume of the vehicle. Animals were fasted 12 hours prior to dosing. Following the period of fasting, the animals were weighed and then the test substance was administered. Three Female animals are used for each group. The dose level of 5, 50, 300 and 2000 mg/kg body weight was administered stepwise. After the substance has been administered, food was withheld for a further 3-4 hours. The principle of laboratory animal care was followed. Observations were made and recorded systematically and continuously as per the guideline after substance administration. The visual observations included skin changes, mobility, aggressively, sensitivity to sound and pain, as well as respiratory movements. Finally, the number of survivors was noted after 24 hrs and these animals were then monitered for a further 14 days and observations made daily. The toxicological effect was assessed on the basis of mortality.

Observations:

Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days, except where they need to be removed from the study and humanely killed for animal welfare reasons or are found dead. It should be determined by the toxic reactions, time of onset and length of recovery period, and may thus be extended when considered necessary. The times at which signs of toxicity appear and disappear are important, especially if there is a tendency for toxic signs to be delayed. All observations are systematically recorded with individual records being maintained for each animal.

Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. The principles and criteria summarized in the Humane Endpoints Guidance Document taken into consideration. Animals found in a moribund condition and animals showing severe pain or enduring signs of severe distress was humanly killed. When animals are killed for human reasons or found dead, the time of death was recorded.

4.5.2. REPEATED DOSE 28-DAY ORAL TOXICITY STUDY OF *SAMUTHARA CHOORANAM*

Test Substance	: **Samuthara chooranam**
Animal Source	: TANUVAS,Madhavaram, Chennai.
Animals	: Wister Albino Rats (Male -24, and Female-24)
Age	**:** 6-8 weeks
Body Weight	**:** 150-200gm.
Acclimatization	**:** Seven days prior to dose.
Veterinary examination	**:** Prior and at the end of the acclimatization period.
Identification of animals	**:** By cage number, animal number and individual marking by using Picric acid
Diet	**:** Pellet feed supplied by Sai meera foods Pvt Ltd,

Bangalore

Water : Aqua guard portable water in polypropylene bottles.

Housing & Environment : The animals were housed in Polypropylene cages provided with bedding of husk.

Housing temperature : between 22ºC ± 3ºC.

Relative humidity : between 30% and 70%,

Air changes : 10 to 15 per hour

Dark and light cycle : 12:12 hours.

Duration of the study : **28 Days.**

Table 4.5.1

Groups	**No of Rats**
Group I Vehicle control (Water)	12(6male,6 female)
Group II low dose X (20mg)	12 (6male,6 female)
Group III STR- Mid dose 5X (100mg)	12 (6male,6female)
Group IV STR- High dose 10X(200mg)	12(6male,6female)

Methodology

Randomization, Numbering and Grouping of Animals:

48 Wistar Albino Rats (24M + 24F) were selected and divided into 4 groups. Each group consist of 12 animals (Male -6, and Female-6). First group treated as a control and other three group were treated with test drug (low, mid, high) for 28 days. Animals were allowed acclimatization period of 7 days to laboratory conditions prior to the initiation of treatment. Each animal was marked with picric acid. The females were nulliparous and non-pregnant.

Justification for Dose Selection:

As per OECD guideline three dose levels were selected for the study. They are low dose (X), mid dose (5X), high dose (10X). X is calculated from the dose (2000 mg) and

the X dose is 20mg/animal, 5X dose is 100mg/animal,10X dose is 200mg/animal.

Preparation and Administration of Dose:

Samuthara chooranam suspended in with water, it was administered to animals at the dose levels of X, 3X, 6X. The test substance suspensions were freshly prepared every two days once for 28 days. The control animals were administered vehicle only. The drug was administered orally by using oral gavage once daily for 28 consecutive days.

Observations:

Experimental animals were kept under observation throughout the course of study for the following:

Body Weight:

Weight of each rat was recorded on day 0, at weekly intervals throughout the course of study.

Food and water Consumption:

Food and water consumed per animal was calculated for control and the treated dose groups.

Clinical signs:

All animals were observed daily for clinical signs. The time of onset, intensity and duration of these symptoms, if any, were recorded.

Mortality:

All animals were observed twice daily for mortality during entire course of study.

Necropsy:

All the animals were sacrificed by excessive anaesthesia on day 29. Necropsy of all animals was carried out.

Laboratory Investigations:

Following laboratory investigations were carried out on day 29 in animals fasted over-night. Blood samples were collected from orbital sinus using sodium heparin (200IU/ml) for Bio chemistry and potassium EDTA (1.5 mg/ml) for Hematology as anticoagulant. Blood samples were centrifuged at 3000 r.p.m. for 10 minutes.

Haematological Investigations:

Haematological parameters were determined using Haematology analyzer.

Biochemical Investigations:

Biochemical parameters were determined using auto-analyzer.

Histopathology:

Control and highest dose group animals will be initially subjected to histopathological investigations. If any abnormality found in the highest dose group than the low, then the mid dose group will also be examined. Organs will be collected from all animals and preserved in 10% buffered neutral formalin for 24 h and washed in running water for 24 h. The organ sliced 5 or 6µm sections and were dehydrated in an auto technicon and then cleared in benzene to remove absolute alcohol. Embedding was done by passing the cleared samples through three cups containing molten paraffin at 50°C and then in a cubical block of paraffin made by the "L" moulds. It was followed by microtome and the slides were stained with Haematoxylin-eosin red.

Statistical analysis:

Findings such as body weight changes, water and food consumption, hematology and blood chemistry were subjected to One-way ANOVA followed by dunnet t test using a computer software programme – Graph pad version 7. All data were summarized in tabular form, (Table-6 to 12).

4.6. PHARMACOLOGICAL STUDY:

IMMUNOMODULATOR ACTIVITY - CELL LINE STUDY

The evaluation of the immunomodulatory activity of Samuthara chooranam was carried out in cultured raw cell line in Biogenix Research Center.

DETERMINATION OF INVITRO IMMUNOMODULATORY EFFECT OF EXTRACTS ON CULTURED RAW CELL LINES

RAW 264.7 cells will be grown to 60% confluence followed by activation with 1 µL lipopolysaccharide (LPS) (1µg/mL). LPS stimulated RAW cells were exposed with different concentration (25, 50, 100 µg/mL) of sample and incubated for 24 hours. After 24 hours of incubation the cells were digested and centrifugation was done at 6000 rpm for 10 minutes. Supernatant was discarded and cells were then resuspented in 200µl of cell lysis buffer (0.1M Tris HCl, 0.25M EDTA, 2M Nacl, 0.5 % Triton x-100). The samples were then kept at 4^0C for 20 minutes. After incubation, the immunomodulatory response was performed by estimating nitrite levels in the cell lysate.

Estimation of Cellular Nitrite Levels

The level of nitrite level was estimated by the method of Lepoivre et al. (Lepoivre et. al. 1990) To 0.5 mL of cell lysate, 0.1 mL of sulphosalicylic acid was added and vortexed well for 30 minutes. The samples were then centrifuged at 5,000 rpm for 15 minutes. The protein-free supernatant was used for the estimation of nitrite levels. To 200 µL of the supernatant, 30 µL of 10% NaOH was added, followed by 300 µL of Tris-HCl buffer and mixed well. To this, 530 µL of Griess reagent was added and incubated in the dark for 10–15 minutes, and the absorbance was read at 540 nm against a Griess reagent blank. Sodium nitrite solution was used as the standard. The amount of nitrite present in the samples was estimated from the standard curves obtained.

4.7. CLINICAL STUDY:

This study was conducted after getting approval from IEC (Institutional Ethical Committee, GSMC Chennai**. IEC No: GSMC-CH-ME-5/011/2016**. This study was also registered in Clinical Trail Registry of India **CTRI No: CTRI/2018/05/013780,** this was done in Post graduate department Sirappu Maruthuvam, Government Siddha Medical College and Hospital, Arignar Anna Hospital Campus, Arumbakkam, Chennai -106 under the observation and guidance of Head of the department.

In this clinical study totally 60 cases were enrolled out of which 20 cases were treated with Internal medicine alone, 20 cases were treated with Internal and External medicines, and 20 cases were treated with Internal, External medicines & Ottradam therapy.

STUDY CENTER:

OPD of Arignar anna Government Hospital of Indian Medicine and Homeopathy, Arumbakkam
Chennai-106.

TRAIL DRUG:

Internal: Samuthara chooranam

External: Vadha noiku veliprayoga thailam

External therapy: Ottradam

Study period: 48 days

Sample Size: 60 cases

20 cases treated with Internal drug alone

20 cases treated with External drug and Ottradam(Therapy)

20 cases treated with Internal, External drug and Ottradam(Therapy)

SUBJECT SELECTION:

There is considerable number of patients reporting of Room no.04, PG Sirappu Maruthuvaum OPD, Aringar anna govt. hospital, GSMC, with the symptom of inclusion

criteria will be subjected to screening test and documented using screening proforma. 60 patients who fulfilled the inclusion criteria were included for the study.

Patients criteria, clinical assessment, siddha assessment, laboratory investigations, diagnosis and treatment aspect in patients after the degree of palliationis achieved theywere advised to visit OPD for further follow up selection were strictly subjected to protocol comprising selection.

INCLUSION CRITERIA:

- Age: 18-60 Years
- Sex: Both male & female (Female dominant disease)
- Low grade fever
- Pain and swelling in interphalangeal joints (mostly in PIP & MCP joints)
- Redness of joint
- Morning stiffness > 1 hr
- Arthritis of 3 or more joints
- Anti CCP +ve
- CRP +ve
- RA factor +ve /-ve
- Patient willing to sign the consent form.

EXCLUSION CRITERIA:

KNOWN CASES OF

- Rheumatic fever
- Psoriatic arthropathica
- Gouty arthritis
- Systemic lupus erythematosus(SLE)
- Progressive systemic sclerosis(PSS)
- History of long term intake of steroids
- DM, SHT, Renal failure
- Carries spine
- Ankylosing spondylitis

- Tumours
- Osteomyelitis
- HIV
- Haemophilia
- Pregnancy and lactation

WITHDRAWAL CRITERIA:

- Intolerance to the drug and development of any serious adverse effect during the period of drug trial.
- Patient turned unwilling to continue in the course of Clinical trial with any other systemic illness**.**

ADR REPORTING:

If ADR is reported, patients will be referred to SCRI (Peripheral Pharmacovigilance centre)

CLINICAL ASSESSMENT:

BLOOD:

Hb

TC

DC

ESR - ½ hr, 1 hr

Blood Sugar-Fasting, PP

Serum Cholesterol

SPECIAL INVESTIGATION:

BT, CT, S.Uric acid

Anti ccp, CRP

URINE:

Albumin

Sugar

Deposits

KIDNEY FUNCTION TEST:

Blood Urea

Serum Creatinine

LIVER FUNCTION TEST:

T. Bilirubin

Serum Alkaline Phosphatase

SGOT

SGPT

STUDY ENROLMENT:

Patient reporting at the OPD with symptoms of Low grade fever, Arthritis of more than 3 joints, Redness, Pain and swelling in PIP & MCP joints, Morning stiffness > 1hr, Subcutaneous nodules, Anti CCP +ve, CRP +ve, RA factor +ve/-ve, are chosen for enrolment based on the inclusion criteria. The patient who are enrolled are informed about the trial drug, possible outcomes and objective of the study in the language and terms understandable to them and the informed consent would be obtained in the consent form.

CONDUCT OF THE STUDY:

Patients satisfying the inclusion and exclusion criteria will be included in the trial. Modern investigations will be carried out before treatment and at the end of the treatment. At the end of the study the trial patients are advised to report when there is recurrence.

DATA COLLECTION FORMS:

Required information will be collected from each patient by using following forms.

Form I : Screening and selection proforma

Form II : History taking proforma

Form III : Clinical assessment on enrollment and on visits proforma

Form IV : Laboratory investigation proforma

Form V : Informed consent form

Form VI : Withdrawal form

Form VII : Patients information sheet

Form VIII : Dietary Advice form

Form IX : Adverse Reaction form

DATA ANALYSIS:

After enrolling the patients in the study, a separate file for each patient will be maintained and all forms will be kept in the file. Whenever the patients visit OPD during the study period necessary entries will be made in the assessment forms. The data entries and adverse events if any will be monitored by the head of the department.

OUTCOME OF TREATMENT:

PRIMARY OUTCOME:

- Primary outcome is mainly assessed by reduction in pain and inflammation of any two joints.
- Reduction of low grade fever and Morning stiffness.
- Pain is assessed by universal pain assessment scale.
- By comparing the any two parameters before and after treatment ESR, Hb, Anti-CCP, CRP.

SECONDARY OUTCOME:

- Secondary outcome is assessed by comparing the safety parameters before and after treatment.

ETHICAL ISSUES:

- Informed consent will be obtained from the patients after explaining about the clinical trial in regional tongue.
- After the consent of the patient (through consent form) if they are in the inclusion criteria they will be enrolled in the study.
- Treatment will be provided free of cost.
- Concomitant medications will be given when required.
- Rescue medications will be given when needed.
- The patients who are excluded (as per exclusion criteria) are given proper treatment with full care at OPD.

RESULTS AND OBSERVATIONS

5. RESULTS AND OBSERVATIONS

ORGANOLEPTIC CHARACTERS

Table –5.1: Organoleptic character of SC

S.NO	CHARACTERS	RESULTS
1.	State	Solid
2.	Appearance	Greenish Brown
3.	Nature	Mild Coarse powder
4.	Taste	Astringent with mild Pungent
5.	Odor	Strong Characteristic

PHYSICOCHEMICAL EVALUATION

Table – 5.2: Physicochemical evaluation of SC

S.No	Parameter	Mean (n=3) SD
1.	***Loss on Drying at 105 °C (%)***	24.67 ± 1.06
2.	***Total Ash (%)***	1.544 ± 0.31
3.	***Acid insoluble Ash (%)***	0.33 ± 0.04
4.	***Water Soluble Ash (%)***	4.46 ± 1.10
5.	***Alcohol Soluble Extractive (%)***	21.22 ± 0.53
6.	***Water soluble Extractive (%)***	9.98 ± 1.15
7.	***PH***	4.5

HEAVY METAL ANALYSIS

Table –5.3: Heavy Metal Analysis of SC

S.NO	Name of the Heavy Metal	Absorption Max Λ max	Result Analysis	Maximum Limit
1.	Mercury	253.7 nm	BDL	1 ppm
2.	Arsenic	193.7 nm	0.268 ppm	3 ppm

BDL- Below Detection Limit

Report and Inference

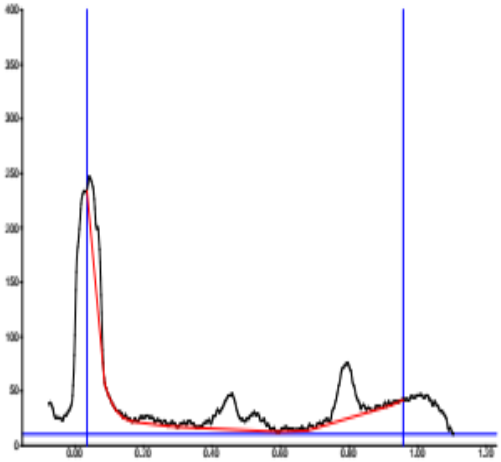
- Results of the present investigation has clearly shows that the sample SC has no traces of Mercury and further shows the presence of Arsenic at 0.268 ppm level and hence it was considered that the heavy metals mercury was absent in the sample SC.
- The reported heavy metal arsenic seems very low (0.268 ppm) when compare to the allowed recommended limit of 3ppm.

TLC AND HPTLC ANALYSIS

TLC Analysis at 254 nm

TLC Analysis at 366 nm

HPTLC finger printing of sample SC



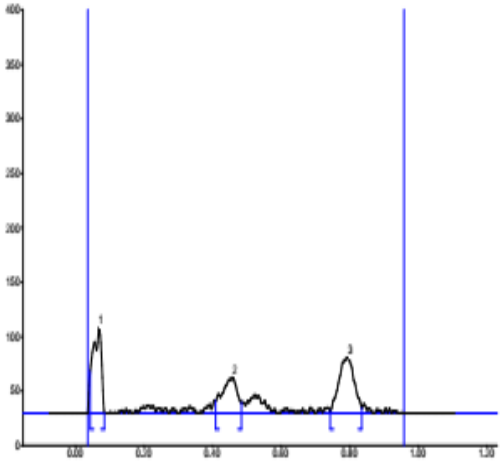


Table – 5.4: HPTLC Analysis of SC

Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %
1	0.04	39.0	0.07	78.7	48.29	0.08	0.4	1461.7	33.99
2	0.41	11.3	0.46	33.0	20.28	0.48	10.2	1089.4	25.33
3	0.74	2.4	0.80	51.2	31.43	0.84	5.0	1749.9	40.69

Report and Inference

HPTLC finger printing analysis of the sample SC reveals the presence of three prominent peaks corresponds to presence of three versatile phytocomponents present with in it. Rf value of the peaks ranges from 0.04 to 0.74. Further the peak 1 occupies the major percentage of area of 48.29 % which denotes the abundant existence of such compound. Followed by this peak 3 and 2 occupies the percentage area of 31.43 and 20.28 %.

PHYTOCHEMICAL ANALYSIS:

Table – 5.5: Phytochemical analysis of SC

S.NO	TEST	OBSERVATION
1.	Alkaloids	-
2.	Flavanoids	+
3.	Glycosides	+
4.	Steroids	+
5.	Triterpenoids	-
6.	Coumarin	-
7.	Phenol	+
8.	Tanin	+
9.	Protein	-
10.	Saponins	+
11.	Sugar	+

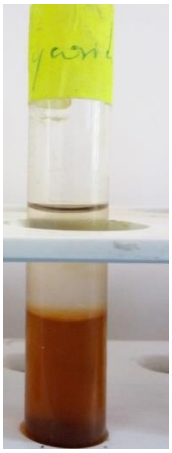
12.	Anthocyanin	-
13.	Betacyanin	-

\+ indicates Presence and - indicates Absence of the Phytocomponents

TESTS DONE FOR

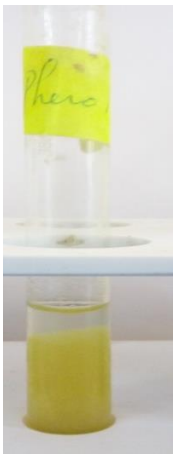
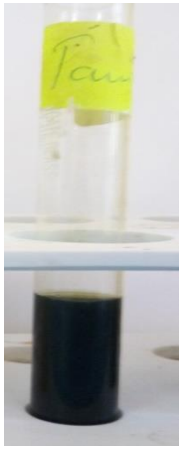
ALKALOIDS **FLAVANOIDS** **GLYCOSIDES** **STEROIDS**



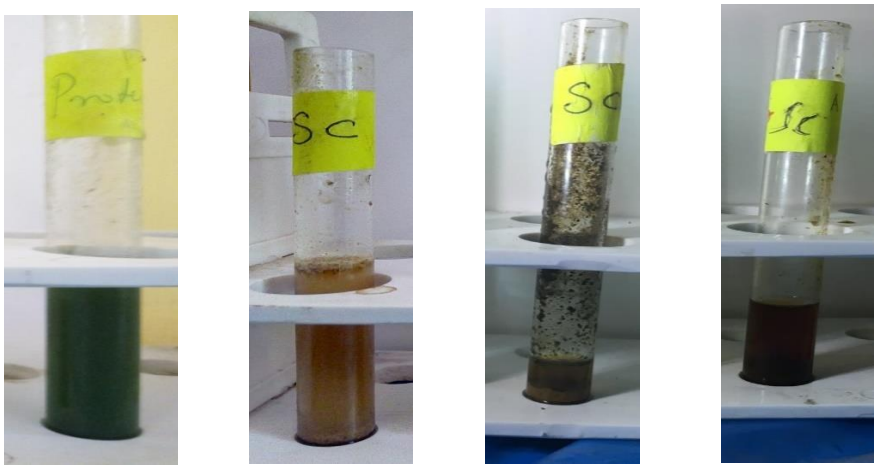



TRITERPENOIDS **COUMARINS** **PHENOL** **TANIN**



PROTEIN **SAPONIN** **SUGAR** **ANTHOCYANIN**



STERILITY TEST BY POUR PLATE METHOD

Observation

No growth was observed after incubation period. Reveals the absence of specific pathogen

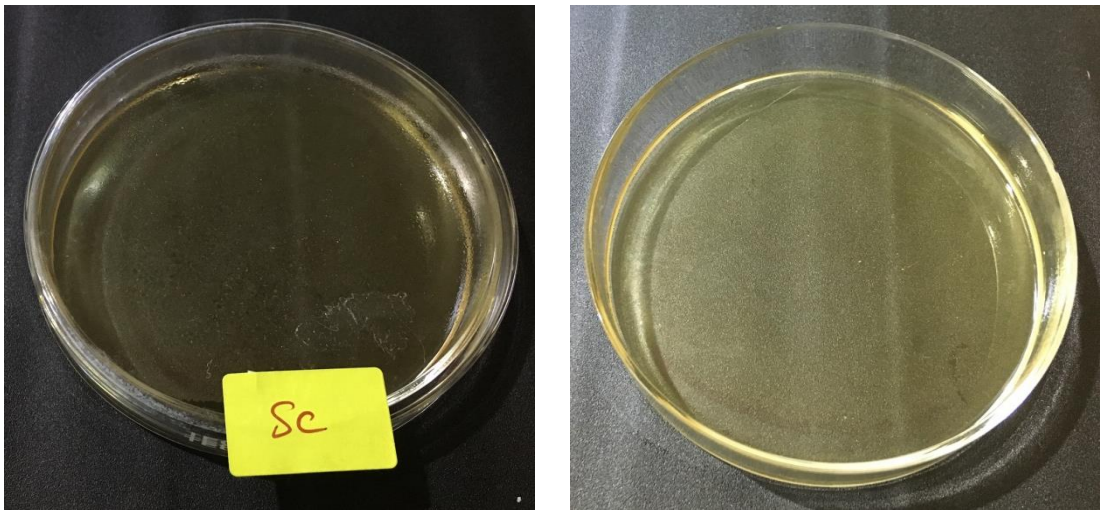


Table – 5.6: Sterility test by Pour Plate Method for SC

Test	Result	Specification	As per AYUSH/WHO
Total Bacterial Count	Absent	NMT 10^5CFU/g	As per AYUSH specification
Total Fungal Count	Absent	NMT 10^3CFU/g	

Result

No growth / colonies was observed in any of the plates inoculates with the test sample.

TOXICOLOGICAL STUDY

Acute oral toxicity study of Samuthara chooranam

Observation done:

Table – 5.7: Dose finding experiment and its behavioral Signs of acute oral Toxicity

SL	Group CONTROL	Observation	SL	TEST GROUP	Observation
1	Body weight	Normal	1	Body weight	Normally
2	Assessments of posture	Normal	2	Assessments of posture	Normal
3	Signs of Convulsion Limb paralysis	Normal	3	Signs of Convulsion Limb paralysis	Absence of sign (-)
4	Body tone	Normal	4	Body tone	Normal
5	Lacrimation	Normal	5	Lacrimation	Absence
6	Salivation	Normal	6	Salivation	Absence
7	Change in skin color	No significant color change	7	Change in skin color	No significant color change
8	Piloerection	Normal	8	Piloerection	Normal
9	Defecation	Normal	9	Defecation	Normal
10	Sensitivity response	Normal	10	Sensitivity response	Normal
11	Locomotion	Normal	11	Locomotion	Normal
12	Muscle gripness	Normal	12	Muscle gripness	Normal
13	Rearing	Mild	13	Rearing	Mild
14	Urination	Normal	14	Urination	Normal

Behaviour:

The animals will be observed closely for behaviour in the first four hours which includes abnormal gait, aggressiveness, exophthalmos, ptosis, akinesia, catalepsy, convolusion, excitation, head twitches, lacrimation, loss of corneal reflex, loss of traction, piloerection reactivity of touch, salivation, scratching, sedation, chewing, head movements, sniffing, straub, tremor and writhes, diarrhea, leathery, sleep and coma.

Body Weight:

Individual weight of animals was determined before the test substance was administered and weights will be recorded at day 1, 7, and 14 of the study. Weight changes were calculated and recorded. At the end of the test, surviving animals were weighed and humanly killed.

Food and water Consumption:

Food and water consumed per animal was calculated for control and the treated dose groups.

Mortality:

Animals were observed for mortality throughout the entire period.

Table – 5.8: Observational study Results

No	Dose mg/kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1.	Control	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2.	2000mg	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-

1.Alertness 2. Aggressiveness 3. Pile erection 4.Grooming 5.Gripping 6.Touch Response 7. Decreased Motor Activity 8. Tremors 9. Convulsions 10. Muscle Spasm 11. Catatonia 12. Muscle relaxant 13. Hypnosis 14. Analgesia 15.Lacrimation 16. Exophthalmos 17. Diarrhea 18. Writhing 19. Respiration 20. Mortality.

(+ Present, - Absent)

Table – 5.9: Body weight Observation

DOSE	DAYS		
	1	7	14
CONTROL	220.6±31.474	221.4 ± 34.324	224.2 ± 27.623
HIGH DOSE	210.5± 27.75	211.7 ± 31.67	213.4 ± 32.67
P value (p)*	NS	NS	NS

Table – 5.10: Water intake (ml/day) of Wistar albino rats group exposed to SC

DOSE	DAYS		
	1	6	14
CONTROL	58.5 ± 6.74	60 ± 9.13	60.4 ± 4.13
HIGH DOSE	60.4 ± 2.33	60.6. ± 1.11	60.9 ± 6.19
P value (p)*	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table -5.11: Food intake (gm/day) of Wistar albino rats group exposed to SC

DOSE	DAYS		
	1	7	14
CONTROL	40.56 ± 9.36	42.6 ± 4.42	41.6 ± 7.46
LOW DOSE	39.4 ± 1.64	39.3 ± 1.22	39.2 ± 6.24

Results:

All data were summarized in tabular form, (Table 6 - 10) showing for each test group the number of animals used, the number of animals displaying signs of toxicity, the number of animals found dead during the test, description of toxic symptoms, weight changes, food and water intake.

SUB ACUTE TOXICITY

Repeated Dose 28- day oral toxic study of Samuthara chooranam

Table – 5.12: Body weight of wistar albino rats group exposed to SC

DOSE	DAYS				
	1	7	14	21	28
CONTROL	220.6 ± 33.673	221.4 ± 40.114	221.7 ± 39.661	222.6 ± 39.73	222.7 ± 41.311
LOW DOSE	180.2 ± 21.124	180.7 ± 33.64	181.4 ± 21.514	182 ± 21.66	182.42 ± 12.76
MID DOSE	176.6 ± 10.64	176.3 ± 22.74	176.4 ± 38.12	178.1 ± 33.36	179.7 ± 23.12
HIGH DOSE	187.4 ± 36.74	187.6 ± 32.72	187.6 ± 32.46	187 ± 22.78	186.92 ± 26.49
P value (p)*	NS	NS	NS	NS	NS

NS- Not Significant, **(p > 0.01),*(p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table – 5.13: Water intake (ml/day) of Wistar albino rats group exposed to SC

DOSE	DAYS				
	1	6	14	21	28
CONTROL	61.5 ± 8.95	61 ± 6.23	58.5 ± 6.23	59 ± 8.196	61.5 ± 3.96
LOW DOSE	56.5 ± 3.31	56.4 ± 3.62	56.7 ± 3.26	56.2 ± 3.29	56.9 ± 3.13
MID DOSE	55.7 ± 4.33	56.3 ± 2.11	57.1 ± 2.43	58.4 ± 2.11	58.4 ± 2.34
HIGH DOSE	60.1 ± 1.32	60.2 ± 2.13	60.7 ± 2.13	65.2 ± 1.73	63.4 ± 2.65
P value (p)*	NS	NS	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table -5.14: Food intake (gm/day) of Wistar albino rats group exposed to SC

DOSE	DAYS				
	2	7	23	22	28
CONTROL	37 ± 5.37	38.5 ± 3.22	39.5 ± 3.37	38.5 ± 3.37	37 ± 3.12
LOW DOSE	43.7 ± 2.98	45.3 ± 1.22	45.1 ± 1.18	45.4 ± 2.12	45.6 ± 2.42
MID DOSE	47.2 ± 3.75	47.2 ± 3.60	47.2 ± 4.25	47.4 ± 2.68	49.2 ± 2.44

HIGH DOSE	46.2 ± 2.34	46.2 ± 2.64	49.6 ± 2.66	48.2 ± 3.20	48.0 ± 3.62
P value (p)*	NS	NS	NS	NS	NS

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table – 5.15: Haematological parameters of Wistar albino rats group exposed to SC

Category	Control	Low dose	Mid dose	High dose	P value (p)*
Haemoglobin (g/dl)	13.8±0.88	13.80±0.66	14.14±0.66	13.28±0.96	N.S
Total WBC ($\times 10^3$ l)	11.91±0.59	11.25±0.73	11.48±0.91	11.20±1.17	N.S
Neutrophils(%)	33.65±0.06	32.23±0.14	35.41±1.36	35.20±2.20	N.S
lymphocyte (%)	70.24±1.48	70.12±3.12	70.20±2.66	70.10±2.16	N.S
Monocyte (%)	0.86±0.07	0.84±0.09	0.82±0.03	0.81±0.06	N.S
Eosinophil (%)	0.54±0.09	0.56±0.02	0.56±0.06	0.57±0.04	N.S
Platelets cells 10^3/µl	687.17±8.76	688.71±8.16	683.18±9.0	687.16±9.74	N.S
Total RBC (10^6/ µl)	7.99±0.12	7.99±0.57	7.82±0.59	8.05±0.72	N.S
PCV%	37.79±0.6	41.35±1.13	43±1.68	45.82±2.54	N.S
MCHC g/Dl	33.6±2.23	35.09±1.29	36.98±1.22	34.03±1.24	N.S
MCV fL (µm^3)	49.07±3.64	50.20±1.22	51.20±1.24	52.24±1.44	N.S

N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table – 5.16: Biochemical Parameters of Wistar albino rats group exposed to SC

BIOCHEMICAL PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
GLUCOSE (R) (mg/dl)	74.45±13.4	76.16±8.44	78.26±11.20	76.42±11.6	N.S
T.CHOLESTEROL (mg/dl)	115.26±1.83	115.45±1.83	116.42±1.78	116.22±1.73	N.S
TRIGLY(mg/dl)	46.35±1.48	46.32±1.48	44.58±1.30	45.66±1.33*	N.S
LDL	73.8±2.43	73.24±2.54	73±2.44	73.64±24.32	NS
VLDL	15.2±2.44	15.42±4.64	15.44±6.64	15.64±34.36	NS
HDL	26.66±6.88	26.86±2.24	26.68±4.66	26.78±21.22	NS
Ratio 1(T.CHO/HDL)	4.42±2.44	4.46±3.14	4.44±8.44	4.46±22.22	NS
Ratio 2(LDL/HDL)	2.83±24.22	2.84±2.22	2.86±2.20	2.66±46.02	NS
Albumin (g/dL)	3.3±0.17	3.43±0.12	3.34±22.02	3.54±6.86	NS

NS- Not Significant, **(p > 0.01), * (p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table – 5.17: Renal function test of Wistar albino rats group exposed to SC

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
UREA (mg/dl)	13.35±0.99	14.31±0.46	14.06±1.38	14.48±1.42	N.S
CREATININE (mg/dl)	0.58±0.08	0.46±0.06	0.62±0.04	0.66±0.02	N.S
BUN (mg/dL)	15.12±0.10	15.10±0.60	16±0.44	16.10±2.12	NS
URIC ACID (mg/dl)	5.37±0.35	5.11±0.43	5.7±1.25*	5.48±0.23	N.S

NS- Not Significant, **(p > 0.01), * (p >0.05) , n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

Table – 5.18: Liver Function Test of Wistar albino rats group exposed to SC

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
T.BILIRUBIN (mg/dl)	0.50±0.07	0.55±0.06	0.59±0.08	0.56±0.05	N.S
SGOT/AST(U/L)	114.95±1.39	116.35±0.51	117.01±1.53	116.55±1.03	N.S
SGPT/ALT(U/L)	71.23±1.28	75.91±1.59	75.34±1.48	74.32±0.68	N.S
ALP(U/L)	146.25±8.77	141±16.17	148.16±24.07*	149.33±14.65*	N.S
T.PROTEIN(g/dL)	6.32±0.38	7.48±0.34	7.016±0.23	6.53±0.46	N.S

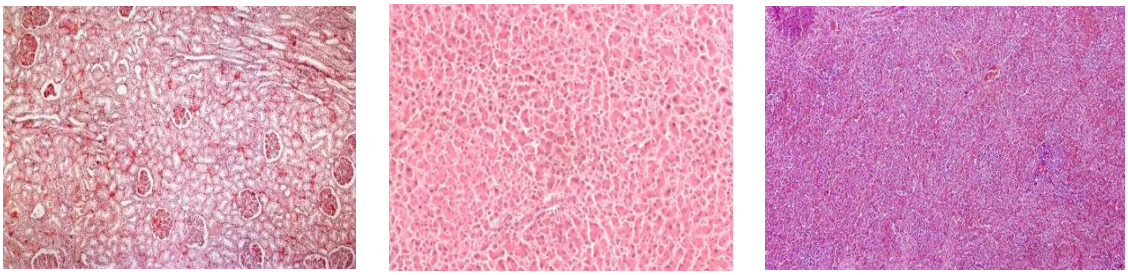
NS- Not Significant, **(p > 0.01), * (p >0.05), n = 10 values are mean ± S.D

(One way ANOVA followed by Dunnett's test)

HISTOPATHOLOGY

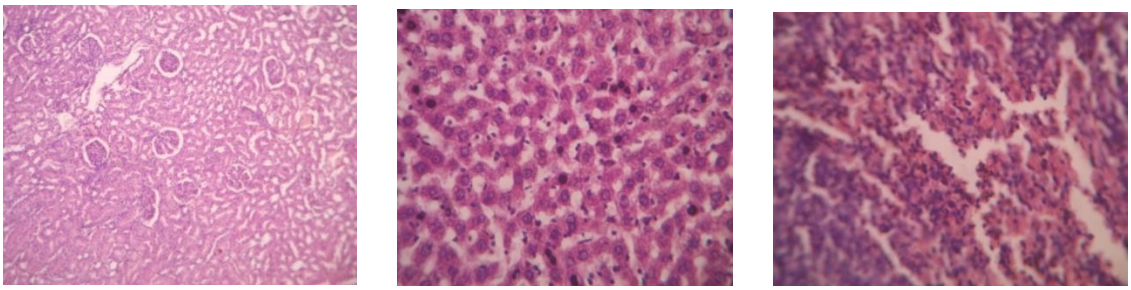
CONTROL GROUP

Kidney Liver Spleen



TEST GROUP (HIGH DOSE)

Kidney Liver Spleen



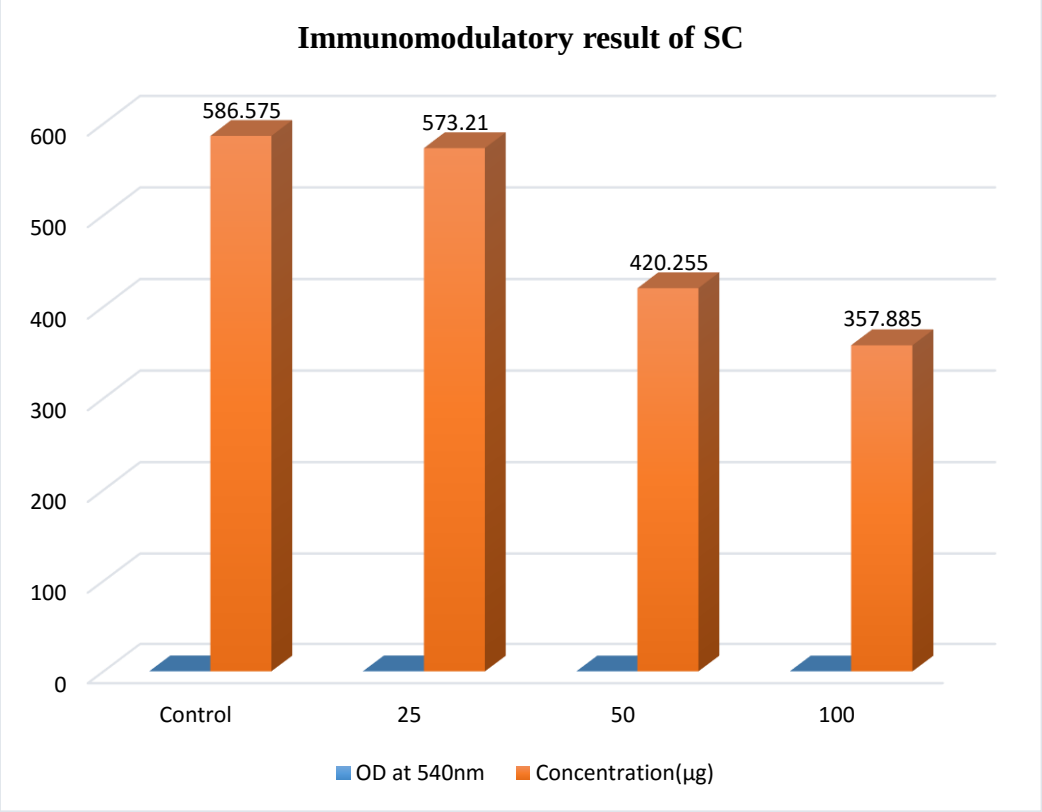
PHARMACOLOGICAL STUDY:

SAMPLE: SAMUTHARA CHOORANAM

Table – 5.19: Immunomodulator activity of SC

Sample Concentration(µg/ml)	OD at 540nm	Concentration(µg)
Control	0.1185	586.575
25	0.1158	573.21
50	0.0849	420.255
100	0.0723	357.885

Chart – 1: Immunomodulatory result of SC



Standard – Nitrate level

Table –5.20: Standard nitrate level for Immunomodulatory activity

Concentration(µg)	OD(540 nm)
100	0.021
200	0.42
300	0.06
400	0.08
500	0.17

Result and Inference:

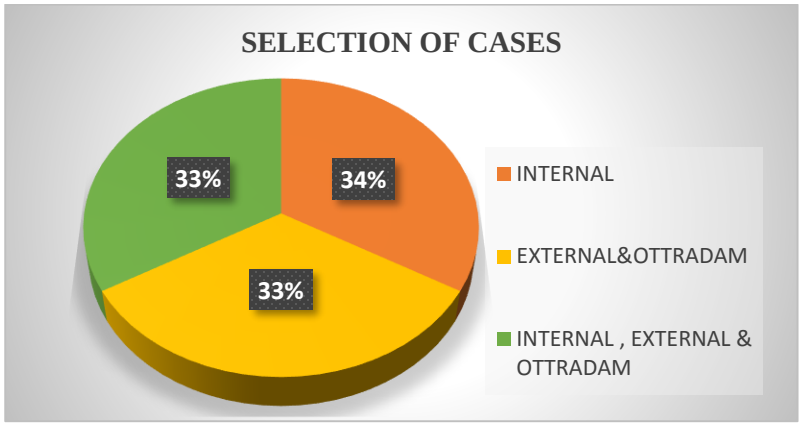
While the concentration level is decreased, nitrate level increased. Hence 25µg/ml of SC has rich level of nitrate and thus proven to be an Immunomodulator.

SELECTION OF CASE:

Table – 5.21: Selection of cases

S.NO	SELECTION OF CASES	NO OF PATIENTS	PERCENTAGE(%)
1.	INTERNAL	20	33.3
2.	EXTERNAL & OTTRADAM	20	33.3
3.	INTERNAL , EXTERNAL & OTTRADAM	20	33.3

Chart - 2: Selection of cases



Inference:

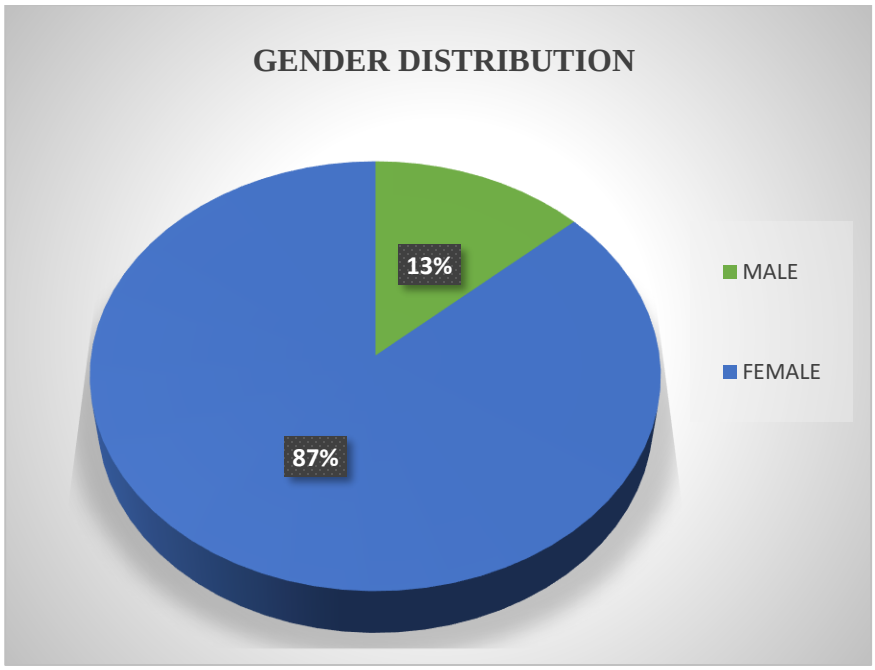
Among 60 cases, 20 cases(34%) were treated with internal drug alone, 20 cases(33%) were treated with external drug & ottradam and 20 cases(33%) were treated with internal, external drug & ottradam.

GENDER DISTRIBUTION:

Table -5.22: Gender distribution

S.NO	GENDER DISTRIBUTION	NO OF PATIENTS	PERCENTAGE(%)
1.	MALE	8	13
2.	FEMALE	52	87

Chart - 3: Gender distribution



Inference:

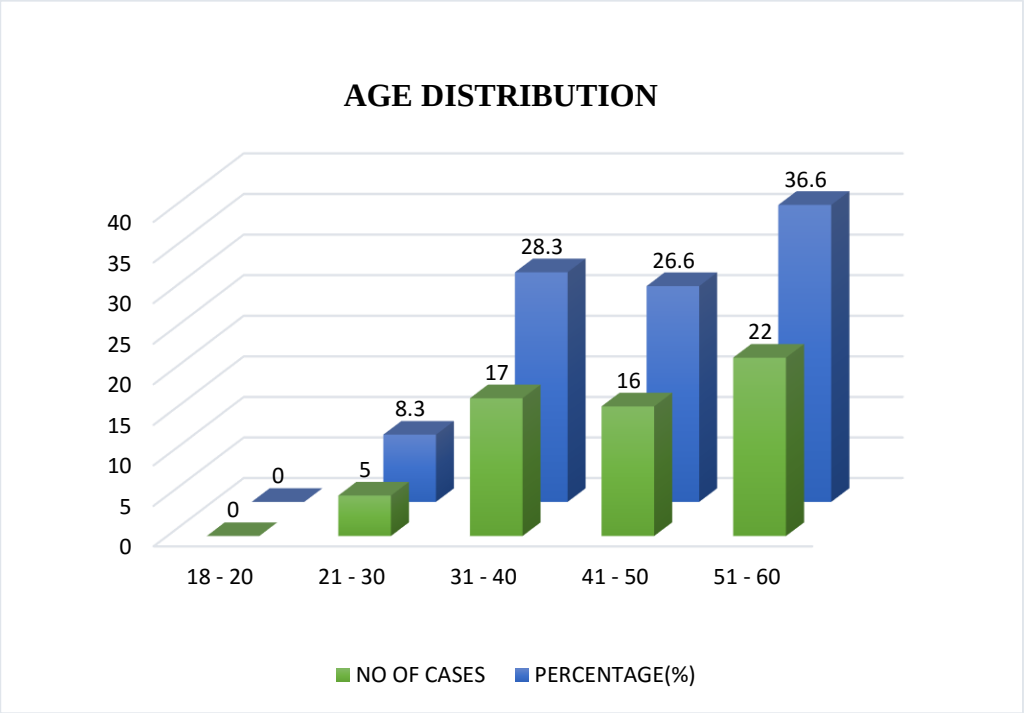
Among 60 cases, 8 cases(13%) were male and 52 cases(87%) were female.

AGE DISTRIBUTION:

Table -5.23: Age distribution

S.NO	AGE DISTRIBUTION	NO OF CASES	PERCENTAGE(%)
1.	18 – 20	0	0
2.	21 – 30	5	8.3
3.	31 – 40	17	28.3
4.	41 – 50	16	26.6
5.	51 – 60	22	36.6

Chart - 4: Age distribution



Inference:

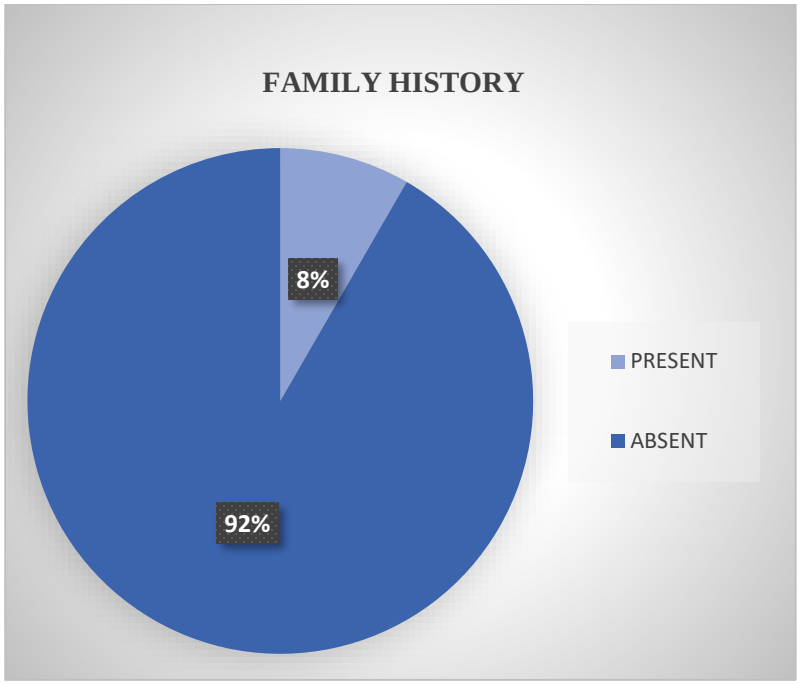
Among 60 cases, high age incidence is between 51-60(36.6%) and 31-40(28.3%).

FAMILY HISTORY:

Table –5.24: Family history

S.NO	FAMILY HISTORY	NO OF CASES	PERCENTAGE(%)
1.	PRESENT	5	8
2.	ABSENT	55	92

Chart - 5: Family history



Inference:

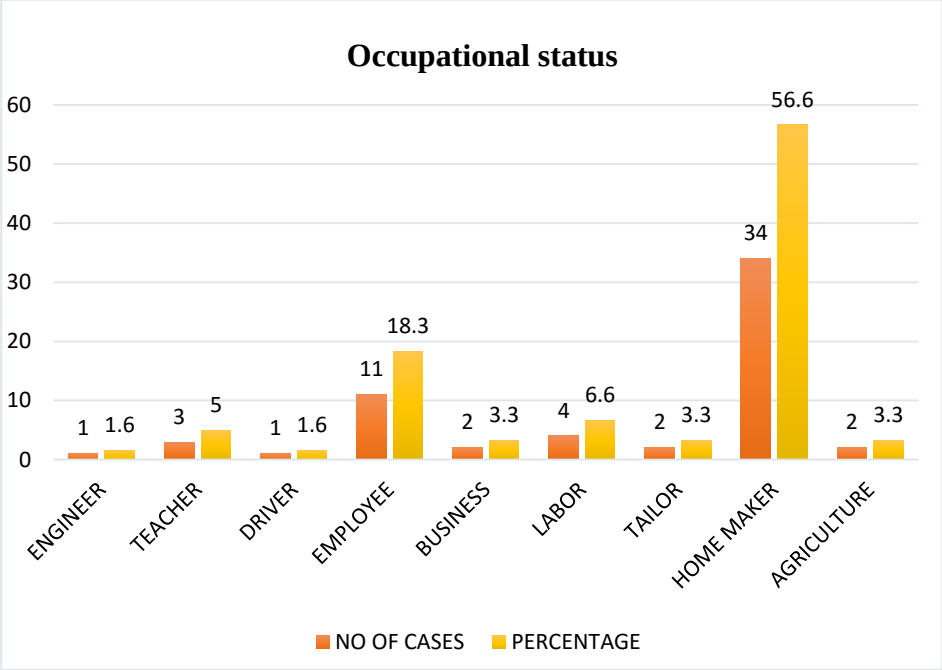
Among 60 cases, only 5 cases(8%) had positive family history of Rheumatoid arthritis.

OCCUPATIONAL STATUS:

Table -5.25: Occupational status

S.NO	OCCUPATIONAL STATUS	NO OF CASES	PERCENTAGE(%)
1.	ENGINEER	1	1.6
2.	TEACHER	3	5
3.	DRIVER	1	1.6
4.	EMPLOYEE	11	18.3
5.	BUSINESS	2	3.3
6.	LABOR	4	6.6
7.	TAILOR	2	3.3
8.	HOME MAKER	34	56.6
9.	AGRICULTURE	2	3.3

Chart - 6: Occupational status



Inference:

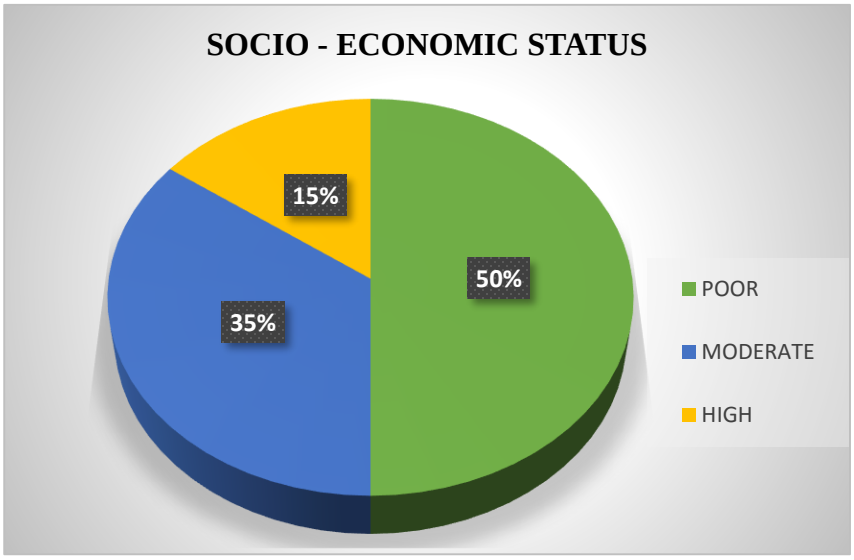
Among 60 cases, 34 cases(56.6%) were Home maker and 11 cases(18.3%) were Employee.

SOCIO – ECONOMIC STATUS:

Table – 5.26: Socio – Economic Status

S.NO	SOCIO – ECONOMIC STATUS	NO OF CASES	PERCENTAGE(%)
1.	POOR	30	50
2.	MODERATE	21	35
3.	HIGH	9	15

Chart - 7: Socio – Economic Status



Inference:

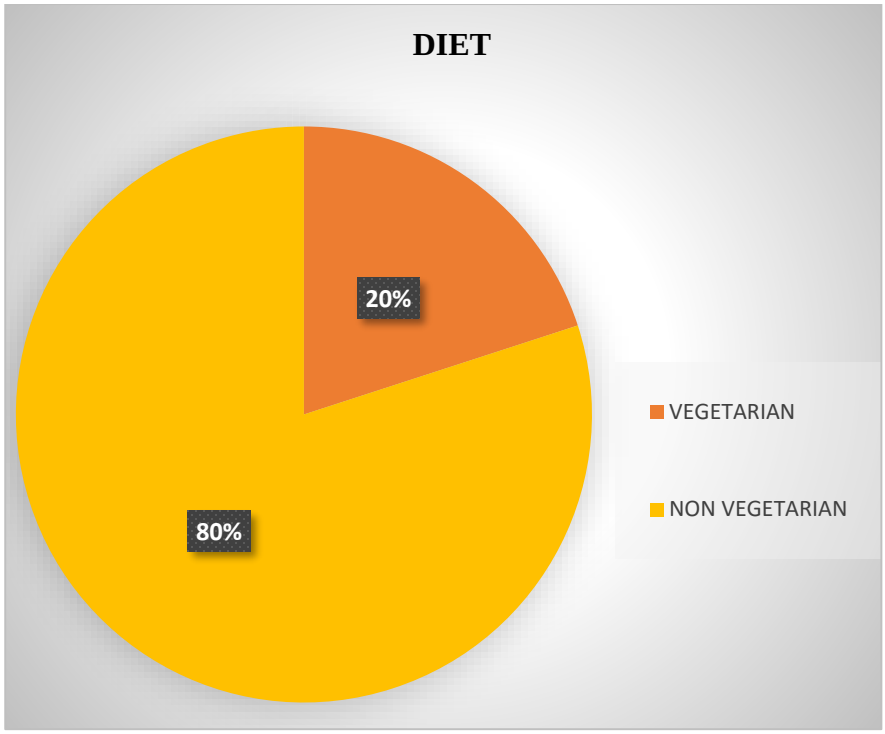
Among 60 cases, 30 cases(50%) were poor, 21 cases(35%) were moderate and 9 cases(15%) were from high class.

DIET:

Table – 5.27: Diet

S.NO	DIET	NO OF CASES	PERCENTAGE(%)
1.	VEGETARIAN	12	20
2.	NON VEGETARIAN	48	80

Chart - 8: Diet



Inference:

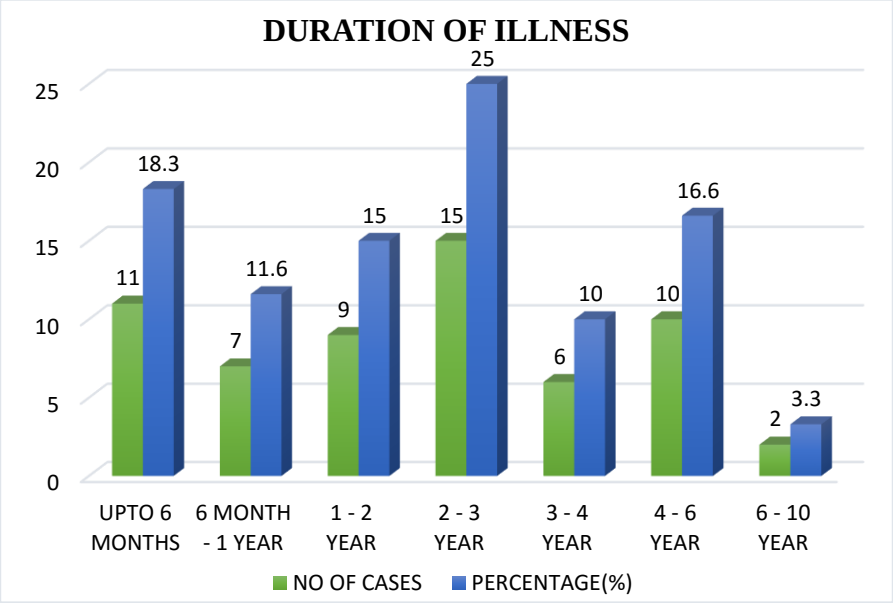
Among 60 cases, 48 cases(80%) were non-vegetarian and 12 cases(20%) were vegetarian.

DURATION OF ILLNESS:

Table – 5.28: Duration of illness

S.NO	DURATION OF ILLNESS	NO OF CASES	PERCENTAGE(%)
1.	UPTO 6 MONTHS	11	18.3
2.	6 MONTH – 1 YEAR	7	11.6
3.	1 – 2 YEAR	9	15
4.	2 – 3 YEAR	15	25
5.	3 – 4 YEAR	6	10
6.	4 – 6 YEAR	10	16.6
7.	6 – 10 YEAR	2	3.3

Chart - 9: Duration of illness



Inference:

Among 60 cases,15 cases(25%) had 2-3 years of illness, 11 cases(18.3%) had 6 months of illness, 10 cases(16.6) had 4-6 years of illness, 9 cases(15%) had 1-2 years of illness, 7 cases(11.6%) had 6 month-1 year of illness, 6 cases(10%) had 3-4 years of illness and 2 cases(3.3%) had 6-10 years of chronic illness.

MODE OF ONSET:

Acute onset: upto 6 months

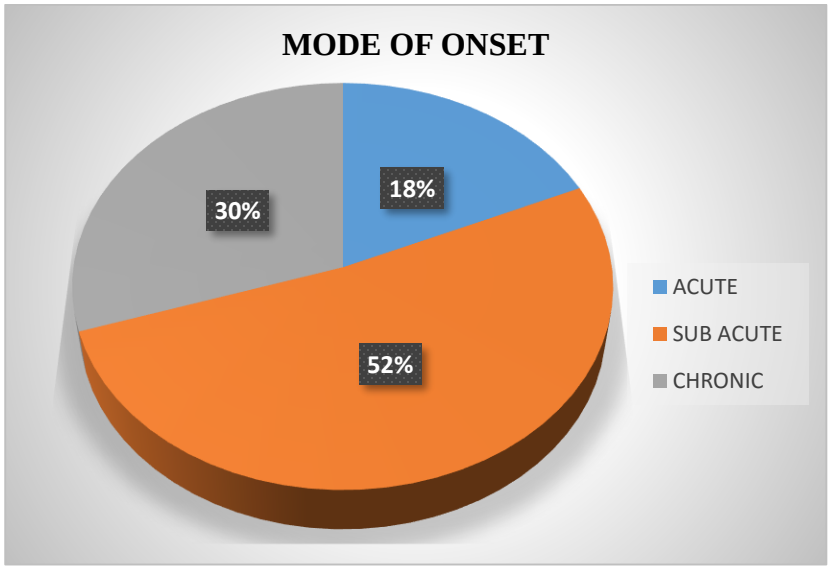
Sub-acute: 6 months – 3 years

Chronic: 4 – 10 years

Table – 5.29: Mode of Onset

S.NO	MODE OF ONSET	NO OF CASES	PERCENTAGE(%)
1.	ACUTE	11	18
2.	SUB ACUTE	31	52
3.	CHRONIC	18	30

Chart - 10: Mode of Onset



Inference:

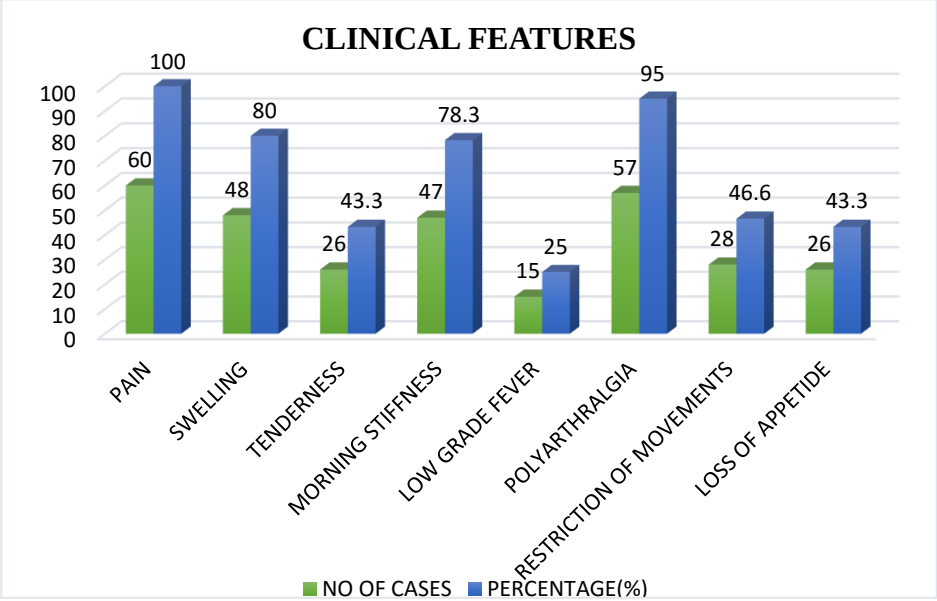
Among 60 cases, 11 cases(18%) were suffering from acute illness, 31 cases(52%) were suffering from sub-acute illness, 18 cases(30%) were suffering from chronic illness.

CLINICAL FEATURES:

Table – 5.30: Clinical Features

S.NO	CLINICAL FEATURES	NO OF CASES	PERCENTAGE(%)
1.	PAIN	60	100
2.	SWELLING	48	80
3.	TENDERNESS	26	43.3
4.	MORNING STIFFNESS	47	78.3
5.	LOW GRADE FEVER	15	25
6.	POLYARTHRALGIA	57	95
7.	RESTRICTED MOVEMENTS	28	46.6
8.	LOSS OF APPETIDE	26	43.3

Chart -11: Clinical features



Inference

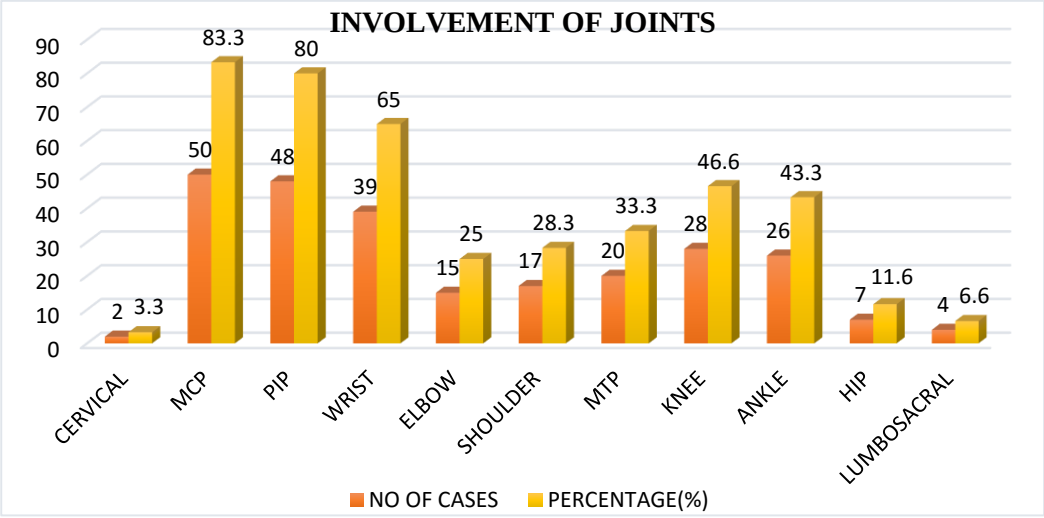
Among 60 cases, 60 cases(100%) had pain, 48 cases(80%) had swelling, 47 cases(78.3%) had morning stiffness, 57 cases(95%) had polyarthralgia, 26 cases(43.3%) had tenderness, 28 cases (46.6%) had restriction of movements, 26 cases(43.3%) had loss of appetide, 15 cases(25%) had low grade fever.

INVOLVEMENT OF JOINTS:

Table -5.31: Involvement of Joints

S.NO	INVOLVEMENT OF JOINTS	NO OF CASES	PERCENTAGE(%)
1.	CERVICAL VERTEBRAE	2	3.3
2.	METACARPO PHALANGEAL JOINT(MCP)	50	83.3
3.	PROXIMAL INTERPHALANGEAL JOINT(PIP)	48	80
4.	WRIST JOINT	39	65
5.	ELBOW JOINT	15	25
6.	SHOULDER JOINT	17	28.3
7.	METATARSAL PHALANGEAL JOINT(MTP)	20	33.3
8.	KNEE JOINT	28	46.6
9.	ANKLE JOINT	26	43.3
10.	HIP JOINT	7	11.6
11.	LUMBOSACRAL JOINT	4	6.6

Chart - 12: Involvement of Joint



Inference:

Among 60 cases, high involvement of joints were MCP and PIP joints, 50 cases(83.3%) and 48 cases(80%) respectively.

RESULTS AFTER TREATMENT:

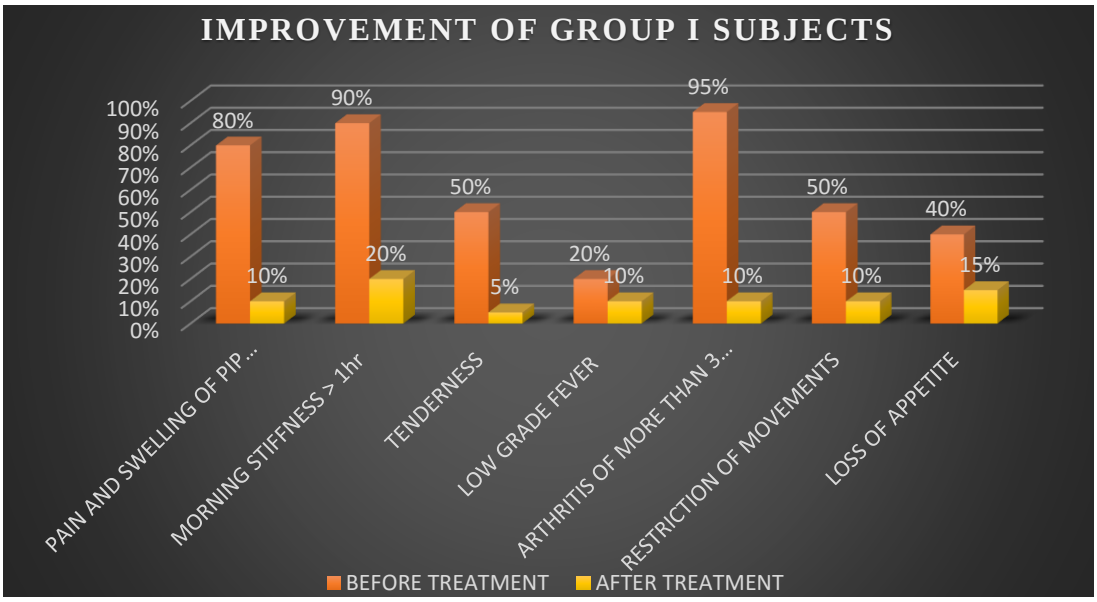
IMPROVEMENT OF GROUP I SUBJECTS:

Improvement in subjects treated with internal trial drug "SAMUTHARA CHOORANAM" in group I subjects

Table –5.32: Improvement of group I subjects

S.NO	CLINICAL FEATURES	BEFORE TREATMENT		AFTER TREATMENT	
		SUBJECTS	PERCENTAGE	SUBJECTS	PERCENTAGE
1.	PAIN AND SWELLING OF PIP JOINT	16	80%	2	10%
2.	MORNING STIFFNESS > 1 hr	18	90%	4	20%
3.	TENDERNESS	10	50%	1	5%
4.	LOW GRADE FEVER	4	20%	2	10%
5.	ARTHRITIS OF MORE THAN 3 JOINTS	19	95%	2	10%
6.	RESTRICTION OF MOVEMENTS	10	50%	2	10%
7.	LOSS OF APPETITE	8	40%	3	15%

Chart – 13: Improvement of group I subject



Inference:

Among 20 cases, 16 cases(80%) had pain and swelling of PIP joints, 18 cases(90%) had morning stiffness > 1hr, 10 cases(50%) had tenderness, 4 cases(20%) had low grade fever, 19 cases(95%) had arthritis of more than 3 joints, 10 cases(50%) had restriction of movements, 8 cases(40%) had loss of appetite before treatment. But after treatment only 2 cases(10%) had pain and swelling of PIP joints, 4 cases(20%) had morning stiffness > 1hr, 1 cases(5%) had tenderness, 2 cases(10%) had low grade fever, 2 cases(10%) had arthritis of more than 3 joints, 2 cases(10%) had restriction of movements, 3 cases(15%) had loss of appetite.

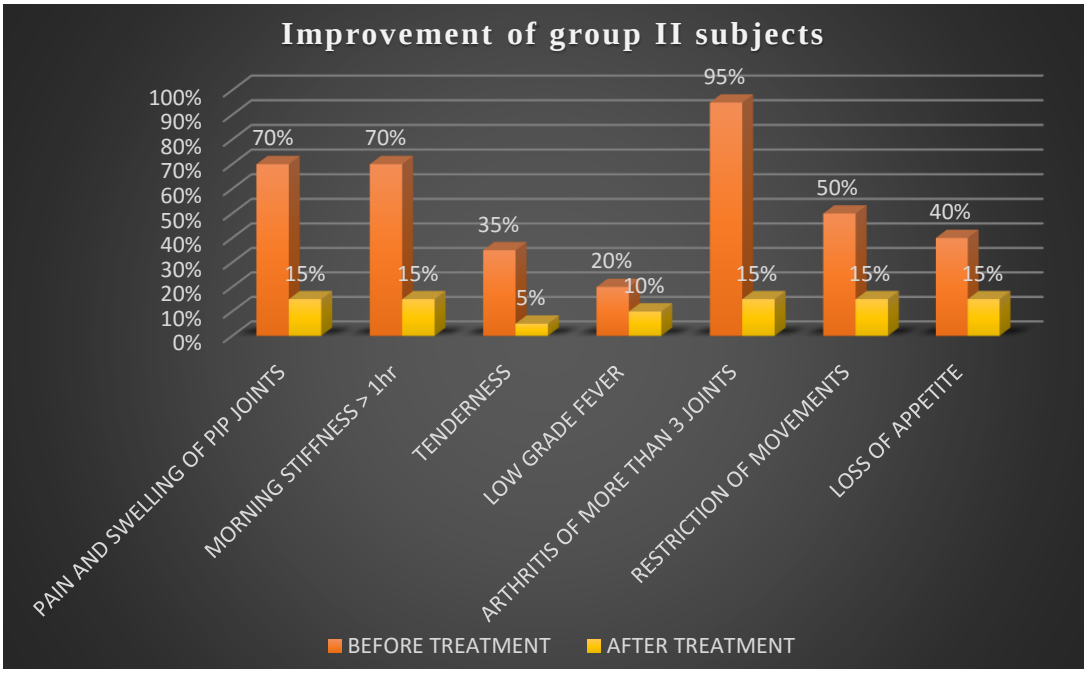
IMPROVEMENT OF GROUP II SUBJECTS:

Improvement in subjects treated with external trial drug "VADHA NOIKU VELIPRAYOGHA THAILAM & OTTRADAM" in group II subjects.

Table – 5.33: Improvement of group II subjects

S. NO	CLINICAL FEATURES	BEFORE TREATMENT		AFTER TREATMENT	
		SUBJECTS	PERCENTAGE	SUBJECTS	PERCENTAGE
1.	PAIN AND SWELLING OF PIP JOINT	14	70%	3	15%
2.	MORNING STIFFNESS > 1 hr	14	70%	3	15%
3.	TENDERNESS	7	35%	1	5%
4.	LOW GRADE FEVER	4	20%	2	10%
5.	ARTHRITIS OF MORE THAN 3 JOINTS	19	95%	3	15%
6.	RESTRICTION OF MOVEMENTS	10	50%	3	15%
7.	LOSS OF APPETITE	8	40%	3	15%

Chart – 14: Improvement of group II subjects



Inference:

Among 20 cases, 14 cases(70%) had pain and swelling of PIP joints, 14 cases(70%) had morning stiffness > 1hr, 7 cases(35%) had tenderness, 4 cases(20%) had low grade fever, 19 cases(95%) had arthritis of more than 3 joints, 10 cases(50%) had restriction of movements, 8 cases(40%) had loss of appetite before treatment. But after treatment only 3 cases(15%) had pain and swelling of PIP joints, 3 cases(15%) had morning stiffness > 1hr, 1 cases(5%) had tenderness, 2 cases(10%) had low grade fever, 3 cases(15%) had arthritis of more than 3 joints, 3 cases(15%) had restriction of movements, 3 cases(15%) had loss of appetite.

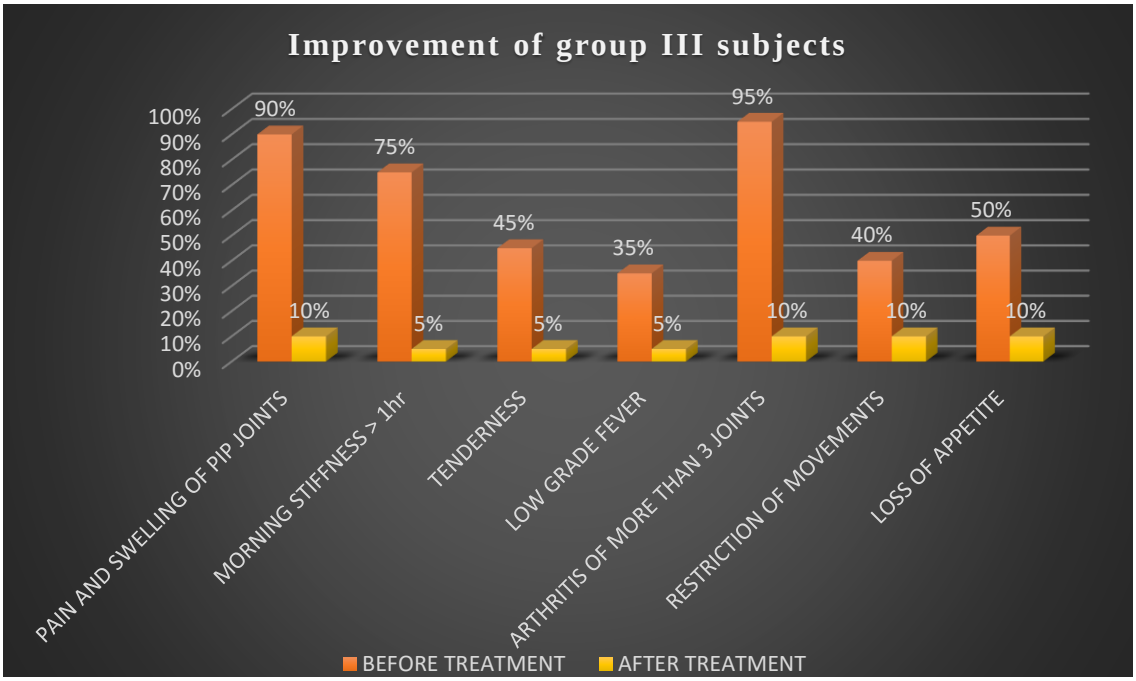
IMPROVEMENT OF GROUP III SUBJECTS:

Improvement in subjects treated with internal and external trial drug "SAMUTHARA CHOORANAM" and "VADHA NOIKU VELIPRAYOGHA THAILAM' respectively & "OTTRADAM" in group III subjects.

Table –5.34: Improvement of group III subjects

S.NO	CLINICAL FEATURES	BEFORE TREATMENT		AFTER TREATMENT	
		SUBJECTS	PERCENTAGE	SUBJECTS	PERCENTAGE
1.	PAIN AND SWELLING OF PIP JOINT	18	90%	2	10%
2.	MORNING STIFFNESS > 1 hr	15	75%	1	5%
3.	TENDERNESS	9	45%	1	5%
4.	LOW GRADE FEVER	7	35%	1	5%
5.	ARTHRITIS OF MORE THAN 3 JOINTS	19	95%	2	10%
6.	RESTRICTION OF MOVEMENTS	8	40%	2	10%
7.	LOSS OF APPETITE	10	50%	2	10%

Chart – 15: Improvement of group III subjects



Inference:

Among 20 cases, 18 cases(90%) had pain and swelling of PIP joints, 15 cases(75%) had morning stiffness > 1hr, 9 cases(45%) had tenderness, 7 cases(35%) had low grade fever, 19 cases(95%) had arthritis of more than 3 joints, 8 cases(40%) had restriction of movements, 10 cases(50%) had loss of appetite before treatment. But after treatment only 2 cases(10%) had pain and swelling of PIP joints, 1 cases(5%) had morning stiffness > 1hr, 1 cases(5%) had tenderness, 1 cases(5%) had low grade fever, 2 cases(10%) had arthritis of more than 3 joints, 2 cases(10%) had restriction of movements, 2 cases(10%) had loss of appetite.

REDUCTION OF PAIN:

SEVERE PAIN: PAIN SCORE 7 – 10

MODERATE PAIN: PAIN SCORE 4 – 6

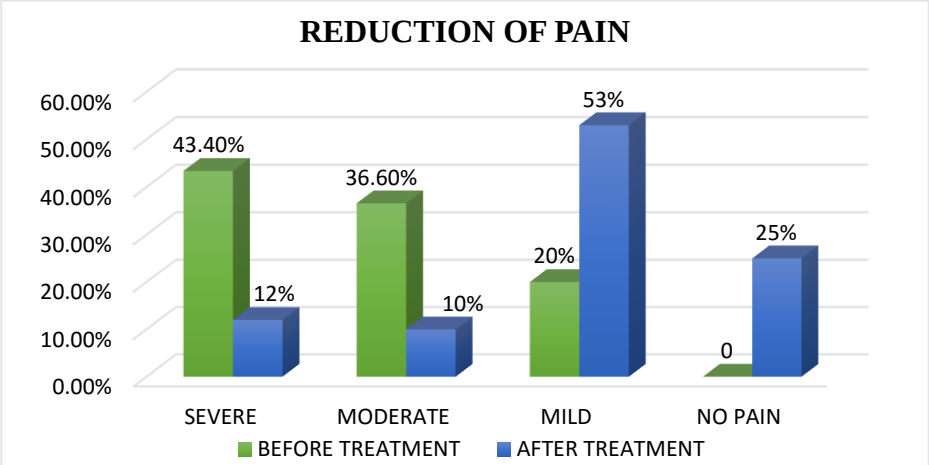
MILD PAIN: PAIN SCORE 1 – 3

NO PAIN: PAIN SCORE 0

Table – 5.35: Reduction of pain

S.NO	REDUCTION OF PAIN	BEFORE TREATMENT		AFTER TREATMENT	
		SUBJECTS	PERCENTAGE (%)	SUBJECTS	PERCENTAGE (%)
1.	SEVERE	26	43.4%	7	12%
2.	MODERATE	22	36.6%	6	10%
3.	MILD	12	20%	32	53%
4.	NO PAIN	0	0	15	25%

Chart – 16: Reduction of pain



Inference:

Among 60 cases, 26 cases(43.4%) had severe pain, 22 cases(36.6%) had moderate pain and 12 cases(20%) had mild pain before treatment. But after treatment only 7 cases(12%) had severe pain, 6 cases(10%) had moderate pain, 32 cases(53%) had mild pain and 15 cases(25%) had no pain.

FUNCTIONAL ABILITY GRADATION:

GRADE I – FIT FOR ALL ACTIVITIES

GRADE II – MILD RESTRICTION

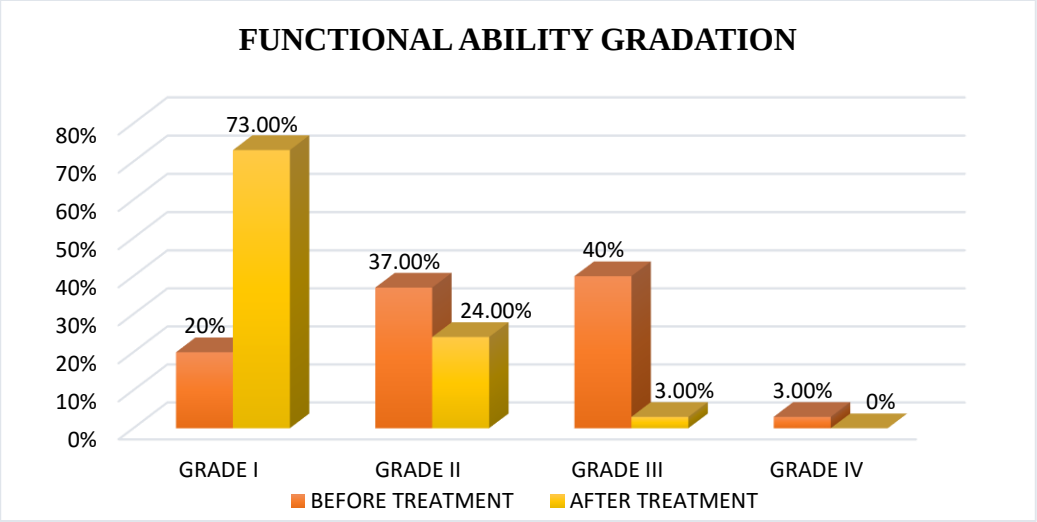
GRADE III – MODERATE RESTRICTION

GRADE IV – CONFINED TO CHAIR OR BED RIDDEN

Table – 5.36: Functional ability gradation

S.NO	GRADE	BEFORE TREATMENT		AFTER TREATMENT	
		SUBJECTS	PERCENTAGE (%)	SUBJECTS	PERCENTAGE (%)
1.	GRADE I	12	20%	44	73%
2.	GRADE II	22	37%	14	24%
3.	GRADE III	24	40%	2	3%
4.	GRADE IV	2	3%	0	0

Chart – 17: Functional ability gradation



Inference:

Among 60 cases, 12 cases(20%) was fit for all activities, 22 cases(37%) had mild restriction in movements, 24 cases(40%) had moderate restriction in movements and 2 cases(3%) had confined to chair on before treatment.

But after treatment, 44 cases(73%) became fit for all activities, 14 cases(24%) had mild restriction in movements, 2 cases(3%) had moderate restriction in movements and no one was confined to chair.

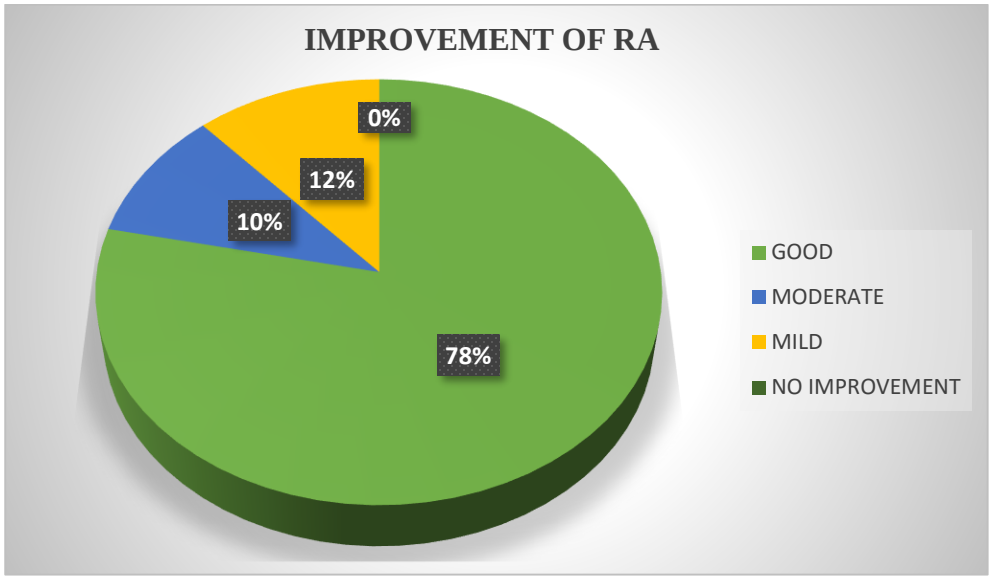
OVERALL RESULT:

IMPROVEMENT OF RA:

Table – 5.37: Improvement of RA

S.NO	IMPROVEMENT	NO OF PATIENTS	PERCENTAGE(%)
1.	GOOD	47	78%
2.	MODERATE	6	10%
3.	MILD	7	12%
4.	NO IMPROVEMENT	0	0

Chart – 18: Improvement of RA



Inference:

Among 60 cases, 47 cases(78%) had good improvement, 6 cases(10%) had moderate improvement and 7 cases(12%) had mild improvement.

GROUP I SUBJECTS: BLOOD INVESTIGATIONS

S. NO	OP. NO	NAME	TC (Cells/ Cu.mm)		DC (%)										ESR (mm/ Hr)				Hb (gm%)	
					N		B		E		M		L		½ hr		1 hr			
			BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
1.	653	AAMINA	7700	8000	58	59	0	0	7	5	0	0	35	36	8	7	16	13	11.2	12.5
2.	3786	SELVAMANI	8000	8700	48	55	0	1	8	7	0	2	44	35	4	4	10	13	11.1	12.3
3.	5791	JOTHI	7500	7700	57	57	0	0	6	4	2	3	35	36	12	11	30	26	13.3	14
4.	6197	PONMALAR	9610	9700	51	65	0	0	3	3	2	1	44	31	25	23	51	48	9.2	10.1
5.	6055	MAALA	6200	6420	47	58	1	1	8	5	3	2	41	34	20	18	45	40	9.1	10.3
6.	6577	VIJAYA	10400	10000	57	66	0	0	7	7	0	2	36	25	36	38	59	56	12.5	14
7.	6988	SUSHILA	9250	9500	67	65	0	1	3	3	4	3	26	28	16	15	37	35	12.6	13
8.	1360	SHANMUGAM	8200	8400	70	68	0	1	5	3	0	2	25	26	21	15	44	30	15.1	15.5
9.	9097	SUGUNA	8700	9100	56	56	1	1	6	7	6	1	31	35	45	40	83	76	9.5	10
10.	450	PREM KUMAR	8600	9000	68	59	0	0	7	4	0	2	25	35	10	9	22	18	15	16
11.	2240	SAIGEETHA	10500	9000	64	58	0	0	8	6	0	2	28	34	18	15	38	30	12.1	13
12.	2683	MANJULA	7800	8000	67	65	1	0	6	3	2	1	24	31	14	12	29	25	10.3	11.5
13.	2685	VIMALA SRI	8300	8500	54	59	1	0	7	4	2	1	36	36	22	21	46	44	9.6	10.2
14.	4069	AMUDHA	7900	8250	56	60	1	0	5	4	2	0	36	36	15	15	32	30	10.9	11.5
15.	4511	SUGANYA	8600	9000	71	67	0	1	6	5	0	1	23	26	5	5	18	15	11.8	13
16.	6512	SHANMUGA SUNDARAM	8700	9200	75	71	0	0	8	6	0	1	17	22	18	14	42	37	11.4	13
17.	7866	VALLI	9400	9500	66	65	1	0	5	5	2	0	26	30	10	9	21	18	11.3	12
18.	9354	SHANTHI	9622	9800	51	59	0	0	2	1	2	0	45	40	25	23	42	38	10.4	11
19	495	SUNDAR	8400	8600	61	67	0	0	6	4	0	0	33	29	10	8	24	16	10.2	11
20.	1086	DURGA DEVI	5600	6300	54	58	0	0	7	4	0	0	39	38	6	6	15	12	11.8	12.4

GROUP II SUBJECTS: BLOOD INVESTIGATIONS

S.NO	OP. NO	NAME	TC (Cells/ Cu.mm)		DC (%)										ESR (mm/ Hr)				Hb (gm%)	
					N		B		E		M		L		½ hr		1 hr			
			BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
1.	656	MALLIKA	9200	7000	51	63	0	0	3	4	1	0	45	33	26	25	43	40	10.3	10.5
2.	793	TAMIL SELVI	8100	8100	55	59	0	1	6	5	3	3	36	32	17	16	23	24	12	11.5
3.	983	R.SUSHEELA	7700	8200	49	60	1	0	6	5	4	0	40	35	9	10	17	19	12	11
4.	1346	KAVERI	8200	7800	53	61	0	0	5	6	3	0	39	33	12	12	25	24	10	11.5
5.	4717	PONN AZHAGU	11000	10500	67	66	0	1	7	7	0	1	26	25	12	11	24	22	10.6	11
6.	4411	MEGALAI	9200	9100	63	59	1	0	7	8	2	0	27	33	7	9	16	18	11	10.5
7.	8324	KANCHANA	8500	8600	50	56	1	0	5	4	4	0	40	40	12	11	27	26	10.4	11
8.	9239	HEMALATHA	9700	9500	53	55	0	1	3	3	1	1	43	40	16	16	35	34	10.2	10.4
9.	9704	GOKILA	8700	8550	53	57	0	0	4	2	0	0	43	41	18	15	29	30	9.3	10
10.	1731	JEEVA	8100	8000	70	65	0	0	5	5	0	0	25	30	14	13	29	26	11.2	12
11.	5249	NIRMALA	9300	9100	65	65	1	0	5	5	3	1	26	29	14	13	33	30	10.3	11
12.	3466	VENKATESAN	8200	8300	58	60	1	0	5	4	1	0	35	36	20	18	35	35	11.6	11
13.	6129	SARASWATHI	9400	9440	65	64	0	0	7	6	1	0	27	30	25	25	43	40	10.4	11
14.	8044	P.VIJAYA	8300	8300	50	56	0	0	5	4	2	2	43	38	10	10	35	30	10.8	12.4
15.	8243	LILLY	3800	4000	79	73	0	0	2	2	0	0	19	25	10	9	22	22	10.4	11.2
16.	8689	YUVARANI	6900	7100	57	64	1	0	6	5	1	1	35	30	15	13	34	28	10.5	11.5
17.	9208	EZHILRANI	6400	6200	68	68	0	0	5	5	2	1	25	26	30	29	60	54	12.7	13
18.	2134	SAVITHRI	7300	7200	64	60	2	0	5	4	2	1	27	35	16	15	31	30	9.6	10.5
19	7648	RADHA	8400	9000	54	59	1	0	7	5	2	1	36	35	22	20	45	43	10.5	11.4
20.	7986	K.SHANTHI	8200	7900	53	60	1	0	8	6	1	0	37	34	9	10	26	24	11.3	12

GROUP III SUBJECTS: BLOOD INVESTIGATIONS

S. NO	OP. NO	NAME	TC (Cells/ Cu.mm)		DC (%)										ESR (mm/ Hr)				Hb (gm%)	
					N		B		E		M		L		½ hr		1 hr			
			BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
1.	5446	JAGADAMBAL	7000	7200	47	62	1	1	7	4	3	2	42	31	11	9	28	26	10	11.4
2.	5718	PRIYANKA	8500	8400	61	61	0	0	6	5	0	2	33	32	5	4	12	12	12.4	13
3.	8134	VASANTHI	15200	14300	71	64	0	0	5	4	0	1	24	31	12	10	40	35	10.2	11.3
4.	3976	PARVATHY	8200	8600	65	63	1	1	3	3	4	2	27	31	6	5	13	10	11	12.5
5.	976	KAVITHA	7200	8000	47	55	1	0	7	5	4	2	41	38	12	10	36	25	9.7	10.5
6.	2315	ABIRAMI	8200	8500	64	60	2	1	3	2	4	1	27	36	7	6	24	20	10.5	11.2
7.	3408	THILAGA	9600	10000	66	67	0	0	6	4	2	1	26	28	19	15	37	30	11.1	11.8
8.	5295	BANUMATHY	10400	10100	69	68	0	0	6	3	0	0	25	29	24	20	47	40	11.4	12
9.	5941	VIJAYARANI	8000	8800	49	55	1	0	6	4	0	0	44	41	15	11	30	23	10.7	11.5
10.	6680	SIVANESAN	10300	10500	70	67	0	1	2	2	8	4	20	26	17	15	45	32	12.9	13.5
11.	7437	JEYANTHI	9800	10000	71	70	0	0	2	2	5	3	22	25	9	9	24	25	11.5	13
12.	25	SARANYA	7200	7600	56	60	1	0	5	4	2	1	36	35	19	16	36	32	11.3	12
13.	315	KRISHNAVENI	8900	9300	70	71	1	0	6	4	1	0	22	25	24	20	47	40	10.8	11.4
14.	1167	KODIARASI	6100	6800	58	63	0	1	4	3	3	1	35	32	30	22	61	46	11.2	12
15.	3629	SELVI	7500	8000	63	67	2	1	6	5	1	0	28	27	21	18	34	36	10.2	11
16.	7633	SIVAKUMAR	7500	8800	58	63	0	0	6	4	0	0	36	33	7	6	23	20	11.6	12
17.	3361	SUNDARI	11700	12000	62	65	0	0	6	5	0	0	32	30	21	19	43	38	8.5	9.5
18.	3288	SALIKA BANU	8900	8600	70	69	0	0	5	3	0	0	25	28	21	20	43	40	9.8	10.3
19	6300	MOHAN BABU	9800	9600	55	61	0	0	8	5	0	0	37	34	5	5	13	12	14.8	15
20.	6363	ROSIE	7500	8200	59	62	0	0	7	6	0	0	34	32	36	33	74	60	12.2	13

GROUP I SUBJECTS: BLOOD INVESTIGATIONS

S. NO	OP. NO	NAME	BLOOD SUGAR				PLT (10^3 ×mm^3)		S. CHOLESTEROL (mg/dl)		S. URIC ACID (mg/dl)		BLEEDING TIME (in mins & secs)		CLOTTING TIME (in mins & secs)	
			FBS		PPBS											
			BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
1.	653	AAMINA	77	80	126	130	236	305	170	181	2.2	2.3	2 & 30	2 & 35	4 & 15	4 & 30
2.	3786	SELVAMANI	82	86	125	132	234	266	189	192	3.5	3.4	2 & 15	2 & 15	5 & 30	5 & 15
3.	5791	JOTHI	76	81	120	126	319	330	152	147	2.2	2.0	3 & 30	3 & 45	6 & 15	6 & 30
4.	6197	PONMALAR	102	100	141	135	280	310	160	151	2.7	2.5	1 & 45	1 & 50	4 & 15	4 & 15
5.	6055	MAALA	81	78	161	150	241	275	146	158	2.6	2.4	2 & 45	2 & 30	5 & 15	5 & 10
6.	6577	VIJAYA	96	90	137	130	234	260	186	183	2.3	3.0	3 & 15	3 & 30	5 & 45	5 & 30
7.	6988	SUSHILA	94	85	135	126	221	239	179	166	4.8	4.4	2 & 15	2 & 20	4 & 35	4 & 35
8.	1360	SHANMUGAM	98	100	143	145	296	306	231	224	4.1	4.0	3 & 30	3 & 20	5 & 15	5 & 10
9.	9097	SUGUNA	77	80	138	140	429	419	179	184	3.5	3.5	2 & 45	2 & 40	4 & 30	4 & 45
10.	450	PREM KUMAR	85	90	129	130	313	316	216	215	3.4	3.4	3 & 15	3 & 30	5 & 30	5 & 30
11.	2240	SAIGEETHA	107	110	207	212	293	310	185	191	2.9	3.0	2 & 10	2 & 10	4 & 30	4 & 10
12.	2683	MANJULA	84	90	143	145	243	251	174	180	4.8	4.9	3 & 15	3 & 20	5 & 30	5 & 15
13.	2685	VIMALA SRI	79	85	128	133	194	215	169	164	2.6	2.5	2 & 30	2 & 15	4 & 15	4 & 15
14.	4069	AMUDHA	88	85	137	130	296	303	173	170	2.4	2.3	2 & 45	2 & 30	4 & 30	4 & 20
15.	4511	SUGANYA	96	100	145	145	322	353	176	171	5.8	5.5	3 & 10	2 & 45	5 & 15	4 & 45
16.	6512	SHANMUGA SUNDARAM	101	110	152	150	242	290	187	184	4.1	4.0	3 & 15	3 & 15	5 & 45	5 & 40
17.	7866	VALLI	89	84	131	120	214	247	193	190	3.5	3.4	2 & 20	2 & 15	4 & 10	4 & 10
18.	9354	SHANTHI	95	90	134	138	247	294	193	205	3.8	3.7	2 & 10	2 & 15	4 & 15	4 & 15
19.	495	SUNDAR	83	80	125	126	212	260	200	205	2.4	2.2	2 & 30	2 & 15	4 & 45	4 & 30
20.	1086	DURGA DEVI	77	70	148	145	264	308	185	190	4.2	4.4	2 & 15	2 & 30	4 & 45	4 & 40

GROUP II SUBJECTS: BLOOD INVESTIGATIONS

S. NO	OP. NO	NAME	BLOOD SUGAR				PLT (10^3 ×mm^3)		S. CHOLESTEROL (mg/dl)		S. URIC ACID (mg/dl)		BLEEDING TIME (in mins & secs)		CLOTTING TIME (in mins & secs)	
			FBS		PPBS											
			BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
1.	656	MALLIKA	103	98	151	143	246	240	163	170	2.7	2.5	2 & 30	2 & 30	4 & 15	4 & 10
2.	793	TAMIL SELVI	83	80	148	135	302	310	187	190	3.7	4.0	2 & 15	2 & 10	5 & 30	5 & 10
3.	983	R.SUSHEELA	98	78	165	143	256	290	133	130	2.5	2.3	2 & 45	2 & 30	4 & 30	4 & 15
4.	1346	KAVERI	100	95	154	148	248	256	145	151	3.0	3.0	2 & 15	2 & 45	4 & 45	4 & 45
5.	4717	PONN AZHAGU	95	100	130	140	341	330	189	188	4.4	4.3	2 & 30	2 & 15	4 & 15	4 & 15
6.	4411	MEGALAI	87	85	141	135	310	351	184	190	3.9	4.0	2 & 15	2 & 30	4 & 30	4 & 45
7.	8324	KANCHANA	78	70	127	110	206	200	163	165	2.2	2.0	2 & 30	2 & 15	4 & 15	4 & 30
8.	9239	HEMALATHA	86	75	130	115	217	215	154	153	2.8	2.5	2 & 15	2 & 30	4 & 35	4 & 30
9.	9704	GOKILA	87	85	128	126	194	196	163	174	2.5	2.5	3 & 15	2 & 45	5 & 30	4 & 45
10.	1731	JEEVA	104	98	155	153	244	250	179	170	3.5	3.1	2 & 20	2 & 30	4 & 15	4 & 30
11.	5249	NIRMALA	79	85	123	141	193	255	184	182	5.4	5.4	2 & 10	2 & 10	4 & 15	3 & 45
12.	3466	VENKATESAN	85	80	145	145	254	240	169	170	4.3	4.2	3 & 10	2 & 45	5 & 15	4 & 30
13.	6129	SARASWATHI	76	86	126	140	278	280	167	170	3.7	3.6	3 & 15	3 & 15	5 & 10	4 & 45
14.	8044	P.VIJAYA	98	85	141	140	315	325	185	181	4.6	4.5	3 & 30	3 & 15	6 & 15	5 & 45
15.	8243	LILLY	102	105	128	132	145	145	270	266	2.6	2.6	2 & 45	2 & 40	5 & 15	5 & 45
16.	8689	YUVARANI	89	90	139	140	269	280	168	170	2.3	2.1	2 & 30	2 & 30	5 & 45	4 & 50
17.	9208	EZHILRANI	82	90	148	151	368	370	174	169	3.8	3.2	2 & 25	2 & 20	4 & 30	4 & 20
18.	2134	SAVITHRI	100	97	140	128	310	305	171	175	3.7	3.5	2 & 20	2 & 15	4 & 45	4 & 30
19.	7648	RADHA	80	80	125	130	320	300	183	182	2.6	2.2	3 & 15	3 & 15	4 & 45	4 & 30
20.	7986	K.SHANTHI	93	95	110	126	336	340	187	183	4.3	4.1	2 & 30	2 & 35	4 & 15	4 & 20

GROUP III SUBJECTS: BLOOD INVESTIGATIONS

S. NO	OP. NO	NAME	BLOOD SUGAR				PLT (10^3 ×mm^3)		S. CHOLESTEROL (mg/dl)		S. URIC ACID (mg/dl)		BLEEDING TIME (in mins & secs)		CLOTTING TIME (in mins & secs)	
			FBS		PPBS											
			BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
1.	5446	JAGADAMBAL	92	100	140	148	250	260	147	155	3.1	3.3	3 & 15	3 & 30	5 & 15	5 & 30
2.	5718	PRIYANKA	100	103	146	145	242	284	170	177	3.6	4.0	2 & 30	2 & 15	4 & 30	4 & 30
3.	8134	VASANTHI	106	98	147	140	302	320	171	163	3.4	3.0	2 & 30	2 & 40	4 & 15	4 & 30
4.	3976	PARVATHY	75	80	125	136	253	294	160	168	3.5	3.5	2 & 10	2 & 10	4 & 15	4 & 10
5.	976	KAVITHA	74	80	136	140	173	210	179	182	3.4	3.2	2 & 40	2 & 35	4 & 30	4 & 15
6.	2315	ABIRAMI	96	100	125	136	185	230	175	171	2.8	2.5	2 & 30	2 & 15	4 & 30	4 & 15
7.	3408	THILAGA	72	81	130	141	187	261	174	178	3.6	3.6	2 & 15	2 & 15	4 & 45	4 & 45
8.	5295	BANUMATHY	92	88	140	138	279	300	195	200	2.5	2.0	2 & 40	2 & 30	4 & 15	3 & 45
9.	5941	VIJAYARANI	84	85	129	135	257	293	176	181	2.8	2.3	2 & 35	2 & 15	4 & 30	4 & 15
10.	6680	SIVANESAN	71	79	130	141	400	450	191	195	5.6	5.2	1 & 50	2 & 10	4 & 10	4 & 30
11.	7437	JEYANTHI	87	96	153	150	366	360	193	205	2.2	2.0	2 & 20	2 & 30	4 & 30	4 & 45
12.	25	SARANYA	94	95	130	145	298	310	164	168	2.7	2.6	2 & 40	2 & 45	4 & 45	4 & 50
13.	315	KRISHNAVENI	81	89	128	138	287	322	155	162	5.9	6.0	2 & 30	2 & 45	6 & 15	5 & 45
14.	1167	KODIARASI	97	91	135	130	220	261	166	169	4.2	4.2	3 & 10	2 & 45	5 & 45	5 & 30
15.	3629	SELVI	78	82	129	138	264	275	176	178	2.5	2.5	2 & 45	2 & 35	5 & 30	5 & 15
16.	7633	SIVAKUMAR	91	100	142	146	268	307	157	160	2.2	2.2	2 & 15	2 & 15	4 & 30	4 & 35
17.	3361	SUNDARI	102	110	200	180	251	278	165	171	3.8	3.6	2 & 45	2 & 30	4 & 45	4 & 30
18.	3288	SALIKA BANU	78	83	137	135	341	360	179	175	4.3	4.2	3 & 30	3 & 10	5 & 30	5 & 15
19.	6300	MOHAN BABU	90	98	102	120	364	350	176	172	3.5	3.2	3 & 15	2 & 45	5 & 30	5 & 15
20.	6363	ROSIE	62	75	103	118	279	291	155	160	4.8	4.5	2 & 45	2 & 15	4 & 15	4 & 20

GROUP I SUBJECTS: RENAL FUNCTION TEST

S.NO	OP.NO	NAME	S. UREA (mg/dl)		S. CREATININE (mg/dl)	
			BT	AT	BT	AT
1.	653	AAMINA	24	22	0.5	0.4
2.	3786	SELVAMANI	22	21	0.8	0.6
3.	5791	JOTHI	18	18	1	0.8
4.	6197	PONMALAR	21	19	0.6	0.5
5.	6055	MAALA	22	19	0.5	0.5
6.	6577	VIJAYA	20	21	0.5	0.4
7.	6988	SUSHILA	14	12	0.6	0.4
8.	1360	SHANMUGAM	15	15	0.6	0.5
9.	9097	SUGUNA	20	20	0.5	0.4
10.	450	PREM KUMAR	18	18	0.7	0.7
11.	2240	SAIGEETHA	25	23	0.6	0.5
12.	2683	MANJULA	21	21	0.5	0.4
13.	2685	VIMALA SRI	24	22	0.7	0.5
14.	4069	AMUDHA	21	21	0.4	0.3
15.	4511	SUGANYA	27	25	0.5	0.4
16.	6512	SHANMUGA SUNDARAM	20	19	0.4	0.4
17.	7866	VALLI	14	15	0.5	0.5
18.	9354	SHANTHI	20	20	0.6	0.5
19.	495	SUNDAR	21	19	0.7	0.6
20.	1086	DURGA DEVI	18	17	0.4	0.4

GROUP II SUBJECTS: RENAL FUNCTION TEST

S.NO	OP.NO	NAME	S. UREA (mg/dl)		S. CREATININE (mg/dl)	
			BT	AT	BT	AT
1.	656	MALLIKA	19	19	0.4	0.5
2.	793	TAMIL SELVI	25	23	0.6	0.5
3.	983	R.SUSHEELA	39	34	1.2	0.8
4.	1346	KAVERI	21	20	0.3	0.4
5.	4717	PONN AZHAGU	22	21	0.4	0.4
6.	4411	MEGALAI	21	20	0.6	0.5
7.	8324	KANCHANA	18	18	0.7	0.6
8.	9239	HEMALATHA	19	18	0.6	0.5
9.	9704	GOKILA	24	22	0.5	0.5
10.	1731	JEEVA	20	19	0.5	0.5
11.	5249	NIRMALA	22	20	0.5	0.4
12.	3466	VENKATESAN	25	22	0.8	0.6
13.	6129	SARASWATHI	27	23	0.6	0.5
14.	8044	P.VIJAYA	19	20	0.9	0.8
15.	8243	LILLY	25	23	0.7	0.7
16.	8689	YUVARANI	23	23	0.4	0.4
17.	9208	EZHILRANI	22	21	0.6	0.6
18.	2134	SAVITHRI	22	20	0.6	0.5
19.	7648	RADHA	22	21	0.5	0.4
20.	7986	K.SHANTHI	18	17	0.4	0.3

GROUP III SUBJECTS: RENAL FUNCTION TEST

S.NO	OP.NO	NAME	S. UREA (mg/dl)		S. CREATININE (mg/dl)	
			BT	AT	BT	AT
1.	5446	JAGADAMBAL	22	21	0.7	0.6
2.	5718	PRIYANKA	20	20	0.4	0.4
3.	8134	VASANTHI	25	22	0.6	0.5
4.	3976	PARVATHY	23	22	0.4	0.4
5.	976	KAVITHA	19	20	0.5	0.4
6.	2315	ABIRAMI	17	17	0.6	0.4
7.	3408	THILAGA	33	29	0.7	0.5
8.	5295	BANUMATHY	24	23	0.6	0.4
9.	5941	VIJAYARANI	14	14	0.3	0.4
10.	6680	SIVANESAN	24	20	0.8	0.7
11.	7437	JEYANTHI	19	19	0.5	0.4
12.	25	SARANYA	21	18	0.5	0.5
13.	315	KRISHNAVENI	20	19	0.4	0.4
14.	1167	KODIARASI	15	16	0.3	0.3
15.	3629	SELVI	18	17	0.4	0.4
16.	7633	SIVAKUMAR	21	19	0.6	0.5
17.	3361	SUNDARI	20	19	0.4	0.4
18.	3288	SALIKA BANU	21	20	0.5	0.4
19.	6300	MOHAN BABU	22	19	0.4	0.5
20.	6363	ROSIE	22	21	0.3	0.3

GROUP I SUBJECTS: LIVER FUNCTION TEST

S.NO	OP.NO	NAME	T. BILIRUBIN (mg/dl)		ALKALINE PHOSPHATASE (U/L)		SGOT (U/L)		SGPT (U/L)	
			BT	AT	BT	AT	BT	AT	BT	AT
1.	653	AAMINA	0.3	0.4	148	147	16	17	13	12
2.	3786	SELVAMANI	0.2	0.2	163	160	23	22	19	19
3.	5791	JOTHI	0.5	0.4	189	187	22	20	20	19
4.	6197	PONMALAR	0.3	0.3	91	90	21	20	30	26
5.	6055	MAALA	0.2	0.2	123	123	25	23	21	20
6.	6577	VIJAYA	0.7	0.5	154	152	22	21	18	16
7.	6988	SUSHILA	0.4	0.3	94	92	18	18	27	24
8.	1360	SHANMUGAM	0.7	0.6	93	90	18	15	29	25
9.	9097	SUGUNA	0.7	0.8	156	158	24	23	20	21
10.	450	PREM KUMAR	0.4	0.3	139	135	37	36	31	31
11.	2240	SAIGEETHA	0.8	0.7	149	150	23	22	18	16
12.	2683	MANJULA	0.4	0.4	210	200	31	28	25	22
13.	2685	VIMALA SRI	0.5	0.5	194	190	25	21	20	18
14.	4069	AMUDHA	0.6	0.5	98	98	19	18	17	16
15.	4511	SUGANYA	0.6	0.4	178	170	36	32	42	38
16.	6512	SHANMUGA SUNDARAM	0.7	0.7	210	198	30	24	35	20
17.	7866	VALLI	0.4	0.3	164	158	24	20	23	21
18.	9354	SHANTHI	0.4	0.4	120	119	24	23	30	27
19.	495	SUNDAR	0.8	0.6	210	195	31	27	35	31
20.	1086	DURGA DEVI	0.5	0.5	160	158	28.2	28	26.2	24

GROUP II SUBJECTS: LIVER FUNCTION TEST

S.NO	OP.NO	NAME	T. BILIRUBIN (mg/dl)		ALKALINE PHOSPHATASE (U/L)		SGOT (U/L)		SGPT (U/L)	
			BT	AT	BT	AT	BT	AT	BT	AT
1.	656	MALLIKA	0.3	0.3	133	131	33	33	21	20
2.	793	TAMIL SELVI	0.4	0.3	139	135	37	36	31	31
3.	983	R.SUSHEELA	0.2	0.2	204	202	31	30	33	31
4.	1346	KAVERI	0.4	0.3	173	173	22	20	17	18
5.	4717	PONN AZHAGU	0.7	0.5	194	189	36	33	30	26
6.	4411	MEGALAI	0.5	0.6	196	200	23	25	20	22
7.	8324	KANCHANA	0.8	0.6	147	143	19	19	22	20
8.	9239	HEMALATHA	0.6	0.5	105	104	13	14	19	16
9.	9704	GOKILA	0.7	0.5	158	148	20	15	22	19
10.	1731	JEEVA	0.7	0.6	159	154	24	22	27	25
11.	5249	NIRMALA	0.4	0.5	188	188	25	26	20	22
12.	3466	VENKATESAN	0.6	0.4	167	162	28	25	22	19
13.	6129	SARASWATHI	0.5	0.6	110	106	19	19	23	23
14.	8044	P.VIJAYA	0.5	0.3	190	183	23	20	19	15
15.	8243	LILLY	0.7	0.5	215	212	35	34	30	28
16.	8689	YUVARANI	0.3	0.4	68	65	22	21	16	15
17.	9208	EZHILRANI	0.4	0.3	155	152	21	19	17	15
18.	2134	SAVITHRI	0.4	0.3	196	193	23	21	20	19
19.	7648	RADHA	0.5	0.4	168	168	27	25	24	24
20.	7986	K.SHANTHI	0.4	0.4	195	194	17	15	19	16

GROUP III SUBJECTS: LIVER FUNCTION TEST

S.NO	OP.NO	NAME	T. BILIRUBIN (mg/dl)		ALKALINE PHOSPHATASE (U/L)		SGOT (U/L)		SGPT (U/L)	
			BT	AT	BT	AT	BT	AT	BT	AT
1.	5446	JAGADAMBAL	0.6	0.6	210	212	31	30	25	25
2.	5718	PRIYANKA	0.4	0.4	192	193	25.7	25	20.6	20
3.	8134	VASANTHI	0.3	0.4	90	90	13	14	17	16
4.	3976	PARVATHY	0.3	0.3	163	164	24	24	21	19
5.	976	KAVITHA	0.6	0.4	175	172	26	25	23	23
6.	2315	ABIRAMI	0.5	0.5	133	134	34	33	22	20
7.	3408	THILAGA	0.3	0.3	153	149	19	20	24	22
8.	5295	BANUMATHY	0.5	0.4	154	150	20	19	23	20
9.	5941	VIJAYARANI	0.4	0.4	98	100	13	14	18	15
10.	6680	SIVANESAN	0.3	0.4	125	124	15	14	9	9
11.	7437	JEYANTHI	0.2	0.2	138	137	24	22	28	24
12.	25	SARANYA	0.3	0.3	183	184	25	22	23	22
13.	315	KRISHNAVENI	0.5	0.5	178	179	13.7	13	11	11
14.	1167	KODIARASI	0.6	0.5	165	163	15	15	19	18
15.	3629	SELVI	0.3	0.3	147	145	25	24	21	20
16.	7633	SIVAKUMAR	0.3	0.4	188	183	31	27	34	30
17.	3361	SUNDARI	0.7	0.5	176	171	30	28	26	23
18.	3288	SALIKA BANU	0.6	0.6	195	188	21	16	19	13
19.	6300	MOHAN BABU	0.5	0.5	187	185	25	24	20	20
20.	6363	ROSIE	0.6	0.4	191	185	33	30	35	27

GROUP I SUBJECTS: URINE ANALYSIS

S.NO	OP.NO	NAME	SUGAR		ALBUMIN		DEPOSITS (Pus cells)	
			BT	AT	BT	AT	BT	AT
1.	653	AAMINA	NIL	NIL	NIL	NIL	1 - 4 cells	1 – 2 cells
2.	3786	SELVAMANI	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 2 cells
3.	5791	JOTHI	NIL	NIL	NIL	NIL	10 – 12 cells	5 – 10 cells
4.	6197	PONMALAR	NIL	NIL	NIL	NIL	2 – 3 cells	1 – 2 cells
5.	6055	MAALA	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 3 cells
6.	6577	VIJAYA	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 2 cells
7.	6988	SUSHILA	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 2 cells
8.	1360	SHANMUGAM	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 4 cells
9.	9097	SUGUNA	NIL	NIL	NIL	NIL	2 – 4 cells	1 – 3 cells
10.	450	PREM KUMAR	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 3 cells
11.	2240	SAIGEETHA	NIL	NIL	NIL	NIL	4 – 6 cells	2 – 5 cells
12.	2683	MANJULA	NIL	NIL	NIL	NIL	2 – 4 cells	2 – 3 cells
13.	2685	VIMALA SRI	NIL	NIL	NIL	NIL	2 – 6 cells	2 – 4 cells
14.	4069	AMUDHA	NIL	NIL	NIL	NIL	1 – 4 cells	1 – 3 cells
15.	4511	SUGANYA	NIL	NIL	NIL	NIL	0 – 1 cells	1 – 2 cells
16.	6512	SHANMUGA SUNDARAM	NIL	NIL	NIL	NIL	2 – 3 cells	0 – 1 cells
17.	7866	VALLI	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 2 cells
18.	9354	SHANTHI	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 2 cells
19.	495	SUNDAR	NIL	NIL	NIL	NIL	2 – 6 cells	2 – 4 cells
20.	1086	DURGA DEVI	NIL	NIL	NIL	NIL	1 – 4 cells	0 – 2 cells

GROUP II SUBJECTS: URINE ANALYSIS

S.NO	OP.NO	NAME	SUGAR		ALBUMIN		DEPOSITS (Pus cells)	
			BT	AT	BT	AT	BT	AT
1.	656	MALLIKA	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 2 cells
2.	793	TAMIL SELVI	NIL	NIL	NIL	NIL	1 – 4 cells	2 – 4 cells
3.	983	R.SUSHEELA	NIL	NIL	NIL	NIL	1 – 3 cells	2 – 3 cells
4.	1346	KAVERI	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 2 cells
5.	4717	PONN AZHAGU	NIL	NIL	NIL	NIL	2 – 5 cells	2 – 4 cells
6.	4411	MEGALAI	NIL	NIL	NIL	NIL	0 – 3 cells	0 – 2 cells
7.	8324	KANCHANA	NIL	NIL	NIL	NIL	1 – 4 cells	0 – 1 cells
8.	9239	HEMALATHA	NIL	NIL	NIL	NIL	2 – 6 cells	1 – 3 cells
9.	9704	GOKILA	NIL	NIL	NIL	NIL	2 – 4 cells	2 – 4 cells
10.	1731	JEEVA	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 2 cells
11.	5249	NIRMALA	NIL	NIL	NIL	NIL	1 – 3 cells	2 – 4 cells
12.	3466	VENKATESAN	NIL	NIL	NIL	NIL	2 – 6 cells	1 – 3 cells
13.	6129	SARASWATHI	NIL	NIL	NIL	NIL	1 – 4 cells	0 – 2 cells
14.	8044	P.VIJAYA	NIL	NIL	NIL	NIL	1 – 3 cells	2 – 4 cells
15.	8243	LILLY	NIL	NIL	NIL	NIL	4 – 7 cells	1 – 3 cells
16.	8689	YUVARANI	NIL	NIL	NIL	NIL	1 – 4 cells	1 – 2 cells
17.	9208	EZHILRANI	NIL	NIL	NIL	NIL	4 – 5 cells	1 – 3 cells
18.	2134	SAVITHRI	NIL	NIL	NIL	NIL	2 – 6 cells	1 – 3 cells
19.	7648	RADHA	NIL	NIL	NIL	NIL	1 – 2 cells	1 - 3 cells
20.	7986	K.SHANTHI	NIL	NIL	NIL	NIL	2 – 4 cells	2 – 4 cells

GROUP III SUBJECTS: URINE ANALYSIS

S.NO	OP.NO	NAME	SUGAR		ALBUMIN		DEPOSITS (Pus cells)	
			BT	AT	BT	AT	BT	AT
1.	5446	JAGADAMBAL	NIL	NIL	NIL	NIL	2 – 4 cells	2 – 3 cells
2.	5718	PRIYANKA	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 3 cells
3.	8134	VASANTHI	NIL	NIL	NIL	NIL	1 – 4 cells	1 – 3 cells
4.	3976	PARVATHY	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 2 cells
5.	976	KAVITHA	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 2 cells
6.	2315	ABIRAMI	NIL	NIL	NIL	NIL	2 – 4 cells	1 – 3 cells
7.	3408	THILAGA	NIL	NIL	NIL	NIL	4 – 6 cells	2 – 5 cells
8.	5295	BANUMATHY	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 3 cells
9.	5941	VIJAYARANI	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 2 cells
10.	6680	SIVANESAN	NIL	NIL	NIL	NIL	2 – 4 cells	1 – 3 cells
11.	7437	JEYANTHI	NIL	NIL	NIL	NIL	2 – 4 cells	2 – 4 cells
12.	25	SARANYA	NIL	NIL	NIL	NIL	2 – 4 cells	0 – 2 cells
13.	315	KRISHNAVENI	NIL	NIL	NIL	NIL	1 – 4 cells	1 – 2 cells
14.	1167	KODIARASI	NIL	NIL	NIL	NIL	2 – 4 cells	1 – 4 cells
15.	3629	SELVI	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 2 cells
16.	7633	SIVAKUMAR	NIL	NIL	NIL	NIL	1 – 2 cells	1 – 3 cells
17.	3361	SUNDARI	NIL	NIL	NIL	NIL	2 - 3 cells	1 – 2 cells
18.	3288	SALIKA BANU	NIL	NIL	NIL	NIL	1 – 3 cells	1 – 3 cells
19.	6300	MOHAN BABU	NIL	NIL	NIL	NIL	1 - 2 cells	2 – 3 cells
20.	6363	ROSIE	NIL	NIL	NIL	NIL	0 cells	0 – 2 cells

GROUP I SUBJECTS: SPECIAL INVESTIGATIONS

S.NO	OP.NO	NAME	CRP		ANTI-CCP	
			BT	AT	BT	AT
1.	653	AAMINA	3.9	2.8	9.9	6.5
2.	3786	SELVAMANI	10.2	8	188.7	183
3.	5791	JOTHI	2.9	1.5	170.6	168
4.	6197	PONMALAR	15	9	200.5	188
5.	6055	MAALA	4.4	2	98.3	94
6.	6577	VIJAYA	26	25	205	203
7.	6988	SUSHILA	35	30	210	203
8.	1360	SHANMUGAM	16	8	200	188
9.	9097	SUGUNA	5.4	6	220	216
10.	450	PREM KUMAR	15	13	482	478
11.	2240	SAIGEETHA	7.3	4	160	150
12.	2683	MANJULA	8.2	4	43	38
13.	2685	VIMALA SRI	13.6	9.3	84	77
14.	4069	AMUDHA	20	15	36	30
15.	4511	SUGANYA	5.3	5	150	142
16.	6512	SHANMUGA SUNDARAM	19	17	45	39
17.	7866	VALLI	9.6	9	68	63
18.	9354	SHANTHI	5.8	5.5	15	8
19.	495	SUNDAR	9	7.5	12	8
20.	1086	DURGA DEVI	7.8	5	30	28

GROUP II SUBJECTS: SPECIAL INVESTIGATIONS

S.NO	OP.NO	NAME	CRP		ANTI-CCP	
			BT	AT	BT	AT
1.	656	MALLIKA	7.8	7.3	310	309
2.	793	TAMIL SELVI	43	40	80.3	75
3.	983	R.SUSHEELA	39	38	110	109
4.	1346	KAVERI	9.1	9	85	81
5.	4717	PONN AZHAGU	12	12	153	146
6.	4411	MEGALAI	15	14	37	36
7.	8324	KANCHANA	29	25	74	69
8.	9239	HEMALATHA	5.6	5	22	18
9.	9704	GOKILA	6.3	4.3	26	21
10.	1731	JEEVA	15	10	48	44
11.	5249	NIRMALA	96	90	110	108
12.	3466	VENKATESAN	48	40	54	48
13.	6129	SARASWATHI	40	36	67	60.3
14.	8044	P.VIJAYA	11	10	48	44
15.	8243	LILLY	40.7	37	135	128
16.	8689	YUVARANI	2.5	2.5	6.2	5
17.	9208	EZHILRANI	48	43	8	4.6
18.	2134	SAVITHRI	12	8	65	60
19.	7648	RADHA	18	15	58	52
20.	7986	K.SHANTHI	9	5	34	28

GROUP III SUBJECTS: SPECIAL INVESTIGATIONS

S.NO	OP.NO	NAME	CRP		ANTI-CCP	
			BT	AT	BT	AT
1.	5446	JAGADAMBAL	31	26	200	184
2.	5718	PRIYANKA	180	178	162.3	155
3.	8134	VASANTHI	30	21	193.8	189
4.	3976	PARVATHY	10.1	7	124	112
5.	976	KAVITHA	24	21	20	9
6.	2315	ABIRAMI	100	98	123	117
7.	3408	THILAGA	35	30	96	88
8.	5295	BANUMATHY	55	43	69	61
9.	5941	VIJAYARANI	8	4	18	11
10.	6680	SIVANESAN	3.7	3	220	214
11.	7437	JEYANTHI	51	49	100	98
12.	25	SARANYA	66	63	140	139
13.	315	KRISHNAVENI	7.6	5	33.9	30
14.	1167	KODIARASI	54	46	130	122
15.	3629	SELVI	26	15	76	71
16.	7633	SIVAKUMAR	25	15	110	103
17.	3361	SUNDARI	36	28	124	116
18.	3288	SALIKA BANU	79	70	188	179
19.	6300	MOHAN BABU	12	5	45	35
20.	6363	ROSIE	15	6	24	15

STATISTICAL ANALYSIS - CLINICAL PROGNOSIS

IMPROVEMENT OF GROUP I SUBJECTS:

Improvement in subjects treated with internal trial drug "SAMUTHARA CHOORANAM" in group I subjects

The most popular non parametric statistical tool, namely, McNemar Test analysis has been employed to analyses the effectiveness with the help of a hypothesis.

IMPROVEMENT OF GROUP I SUBJECTS

S. No	Clinical features	Before Treatment	After Treatment
		n%	n%
1.	PAIN AND SWELLING OF PIP JOINT	16(80)	2(10)**
2.	MORNING STIFFNESS > 1 hr	18(90)	4(20)**
3.	TENDERNESS	10(50)	1(5)**
4.	LOW GRADE FEVER	4(20)	2(10)*
5.	ARTHRITIS OF MORE THAN 3 JOINTS	19(95)	2(10)**
6.	RESTRICTION OF MOVEMENTS	10(50)	2(10)**
7.	LOSS OF APPETITE	8(40)	3(15)*

McNemat test, C.I: 95%, *P<0.05; **P<0.01

Software: spss17 version

Number of cases: 20

Inference:

Since the p value is significant in all clinical features. So there is significant reducing of clinical features among the patients for the treatment of Uthiravadha Suronitham (Rheumatoid Arthritis). Hence it is concluded that the treatment was effective and **significant.**

IMPROVEMENT IN GROUP II SUBJECTS:

Improvement in subjects treated with external trial drug "VADHA NOIKU VELIPRAYOGHA THAILAM & OTTRADAM" in group II subjects

The most popular non parametric statistical tool, namely, McNemar Test analysis has been employed to analyses the effectiveness with the help of a hypothesis.

IMPROVEMENT OF GROUP II SUBJECTS

S. No	Clinical features	Before Treatment	After Treatment
		n%	n%
1.	PAIN AND SWELLING OF PIP JOINT	14(70)	3(15)**
2.	MORNING STIFFNESS > 1 hr	14(70)	3(15)**
3.	TENDERNESS	7(35)	1(5)*
4.	LOW GRADE FEVER	4(20)	2(10)*
5.	ARTHRITIS OF MORE THAN 3 JOINTS	19(95)	3(15)**
6.	RESTRICTION OF MOVEMENTS	10(50)	3(15)*
7.	LOSS OF APPETITE	8(40)	3(15)*

McNemat test, C.I: 95%, *P<0.05; **P<0.01

Software: spss17 version

Number of cases: 20

Inference:

Since the p value is significant in all clinical features. So there is significant reducing of clinical features among the patients for the treatment of Uthiravadha Suronitham (Rheumatoid Arthritis). Hence it is concluded that the treatment was effective and **significant.**

IMPROVEMENT IN GROUP III SUBJECTS:

Improvement in subjects treated with internal and external trial drug "SAMUTHARA CHOORANAM" and "VADHA NOIKU VELIPRAYOGHA THAILAM' respectively & "OTTRADAM" in group III subjects.

The most popular non parametric statistical tool, namely, McNemar Test analysis has been employed to analyses the effectiveness with the help of a hypothesis.

IMPROVEMENT OF GROUP III SUBJECTS

S. No	Clinical features	Before Treatment	After Treatment
		n%	n%
1.	PAIN AND SWELLING OF PIP JOINT	18(90)	2(10)**
2.	MORNING STIFFNESS > 1 hr	15(75)	1(5)**
3.	TENDERNESS	9(45)	1(5)**
4.	LOW GRADE FEVER	7(35)	1(5)*
5.	ARTHRITIS OF MORE THAN 3 JOINTS	19(95)	2(10)**
6.	RESTRICTION OF MOVEMENTS	8(40)	2(10)*
7.	LOSS OF APPETITE	10(40)	2(10)*

McNemat test, C.I: 95%, *P<0.05; **P<0.01

Software: spss17 version

Number of cases: 20

Inference:

Since the p value is significant in all clinical features. So there is significant reducing of clinical features among the patients for the treatment of Uthiravadha Suronitham (Rheumatoid Arthritis). Hence it is concluded that the treatment was effective and **significant.**

Group I Subjects :Liver Function Test

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
2	SGPT	24.96±7.37	22.3±6.18	**<0.05**
3	SGOT	24.86±5.76	22.90±5.14	**<0.001**
4	Alkaline Phosphatase	152.15±39.59	148.5±36.73	**<0.05**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

Group II Subjects :Liver Function Test

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
2	SGPT	22.6±5.01	21.2±5.05	**<0.05**
3	SGOT	24.90±6.60	23.60±6.63	**<0.05**
4	Alkaline Phosphatase	163.00±37.75	160.10±38.23	**<0.001**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

Group III Subjects :Liver Function Test

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
2	SGPT	21.93±6.23	19.85±5.19	**<0.001**
3	SGOT	23.17±6.77	21.95±6.11	**<0.05**
4	Alkaline Phosphatase	162.05±32.39	160.40±31.64	**<0.05**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP I SUBJECTS :RFT

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	Urea	20.25±3.44	19.35±3.01	**<0.05**
2	Creatinine	0.58±0.14	0.48±0.11	**<0.001**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP II SUBJECTS :RFT

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	Urea	22.65±4.60	21.20±3.50	**<0.001**
2	Creatinine	0.59±0.20	0.52±0.13	**<0.05**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP III SUBJECTS :RFT

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	Urea	21.00±4.01	19.75±3.05	**<0.05**
2	Creatinine	0.49±0.14	0.44±0.09	**<0.05**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP I SUBJECTS: BLOOD INVESTIGATION

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	Hb	11.42±1.69	12.31±1.70	**<0.001**
2	ESR1hr	35.20±17.44	31.00±16.51	**<0.001**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP II SUBJECTS: BLOOD INVESTIGATION

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	Hb	10.75±0.84	11.22±0.72	**<0.05**
2	ESR1 hr	31.60±10.45	29.95±8.95	**<0.05**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP III SUBJECTS:BLOOD INVESTIGATION

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	Hb	11.09±1.34	11.89±1.23	**<0.001**
2	ESR1 hr	35.50±15.72	30.10±12.46	**<0.001**

C.I: 95%; Paired samples t test. Where p<0.001, p<0.05 represents statistically significant.

GROUP I SUBJECTS: SPECIAL INVESTIGATIONS

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	CRP	11.97±8.20	9.33±7.47	**<0.001**
2	Anti CCP	131.40±112.95	125.52±112.63	**<0.001**

C.I: 95%; Paired samples t test. Where $p<0.001$, $p<0.05$ represents statistically significant.

GROUP II SUBJECTS: SPECIAL INVESTIGATIONS

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	CRP	25.35±22.85	22.55±21.45	**<0.001**
2	Anti CCP	76.52±67.80	72.29±68.11	**<0.001**

C.I: 95%; Paired samples t test. Where $p<0.001$, $p<0.05$ represents statistically significant.

GROUP III SUBJECTS: SPECIAL INVESTIGATIONS

S.No.	Investigations	Before Treatment Mean±SD n= 20	After Treatment Mean±SD n= 20	P value
1	CRP	42.42±41.30	36.65±41.99	**<0.001**
2	Anti CCP	109.85±62.83	102.40±62.78	**<0.001**

C.I: 95%; Paired samples t test. Where $p<0.001$, $p<0.05$ represents statistically significant.

DISCUSSION

6. DISCUSSION

Rheumatoid arthritis(RA) is a chronic inflammatory syndrome with a strong autoimmune component(autoantigens) are neither tissue nor organ-specific, but comprise a broad collection of post-translational modified proteins, such as citrullinated proteins. Both innate and adaptive mechanisms will closely interplay to promote chronic inflammation in peripheral joints (PIP, MCP, MTP & Wrist joints) more often and very rarely after the larger joints.

The disease **Rheumatoid arthritis** signs and symptoms were correlates with the symptoms of **Uthiravadha Suronitham** mentioned in the siddha literature **Yugi Vaithiya Chindhamani.**

The drugs in the **SAMUTHARA CHOORANAM** and **VADHA NOIKU VELIPRAYOGHA THAILAM** possesses **anti-vadha** and **anti-spasmodic** actions as indicated in the siddha literature Gunapadam-Mooligai & Thadhu Seeva Vagupu were selected as Internal and External medicines respectively for the clinical evaluation on Uthiravadha Suronitham (Rheumatoid arthritis).

After getting proper **Authentication** from the Head of the Department of Medicinal Botany & Gunapadam (Pharmacology) and after conducting the proper analysis of **Toxicological & Pharmacological study** for the Internal trial medicine (Samuthara Chooranam), the medicine was administered to the patients.

60 patients were admitted for the trial in the outpatient ward (Room No:4). Out of which 20 patients was treated with Internal medicine alone (Group I), 20 patients was treated with External medicine with Ottradam(Group II), 20 patients was treated with Internal, External medicine & Ottradam(Group III) and guided by the **Head of the Department of Sirappu Maruthuvam**, **GSMC, Chennai-106.**

Progress of the patients was followed and documented regularly. Various criteria like Distribution of Gender, Age, Diet, Occupational & Socio-Economic status were assessed. Clinical manifestation and assessment of the enhancement in the prognosis of the disease(RA) with the trial drugs along with ottradam were taken into account for evaluating the **Efficacy** of the trial drugs.

GENDER:

13.3% of Patients were in the gender of male

86.7% of Patients were in the gender of female

AGE:

8.3% of Patients were in the age group of 21-30

28.3% of Patients were in the age group of 31-40

26.6% of Patients were in the age group of 41-50

36.6% of Patients were in the age group of 51-60

OCCUPATIONAL STATUS:

56.6% of Patients was Homemakers were affected

18.3% of Patients was Employees were affected

6.6% of Patients was Labours were affected

Mostly Homemakers and Employees were affected

SOCIO-ECONOMIC STATUS:

50% of Patients were affected in the socio-economic status of lower income group because of the low nutrition, poor hygiene and poor immunity.

DIET:

80% of Patients were Non-vegetarian and only 20% of Patients were Vegetarian.

DURATION OF ILLNESS:

25% of Patients had illness for 2-3 years

18.3% of Patients had illness upto 6 months

16.6% of Patients had illness for 4-6 years

15% of Patients had illness for 1-2 years

11.6% of Patients had illness for 6 months – 1 year

10% of Patients had illness for 3-4years

3.3% of Patients had illness for 6-10 years

MODE OF ONSET:

51.6% of Patients were in the Sub-acute stage of the disease (6 month – 3 years)

CLINICAL FEATURES:

80% of Patients merely have all the above said clinical features of the presenting illness.

CLINICAL PROGRESS WITH INTERNAL MEDICINE:

80% of Patients got relief from Pain, Morning stiffness, Inflammation and Restriction of movements.

About 70-75% of Patients had the progress in their clinical features when treated with providing Internal medicine alone.

CLINICAL PROGRESS WITH EXTERNAL MEDICINE AND OTTRADAM:

75% of Patients got relief from Pain, Morning stiffness, Inflammation and Restriction of movements.

About 65-70% of Patients had the progress in their clinical features when treated with providing External medicine and Ottradam.

CLINICAL PROGRESS WITH INTERNAL, EXTERNAL MEDICINE AND OTTRADAM:

80% of Patients got relief from Pain, Morning stiffness, Inflammation and Restriction of movements.

About 70-75% of Patients had the progress in their clinical features when treated with providing Internal medicine, External medicine and Ottradam.

RESULTS:

GROUP I SUBJECTS (INTERNAL MEDICINE):

Among 20 cases, 16 cases(80%) had pain and swelling of PIP joints, 18 cases(90%) had morning stiffness > 1hr, 10 cases(50%) had tenderness, 4 cases(20%) had low grade fever, 19 cases(95%) had arthritis of more than 3 joints, 10 cases(50%) had restriction of movements, 8 cases(40%) had loss of appetite before treatment. But after treatment only 2 cases(10%) had pain and swelling of PIP joints, 4 cases(20%) had morning stiffness > 1hr, 1 cases(5%) had tenderness, 2 cases(10%) had low grade fever, 2 cases(10%) had arthritis of more than 3 joints, 2 cases(10%) had restriction of movements, 3 cases(15%) had loss of appetite.

GROUP II SUBJECTS (EXTERNAL MEDICINE AND OTTRADAM):

Among 20 cases, 14 cases(70%) had pain and swelling of PIP joints, 14 cases(70%) had morning stiffness > 1hr, 7 cases(35%) had tenderness, 4 cases(20%) had low grade fever, 19 cases(95%) had arthritis of more than 3 joints, 10 cases(50%) had restriction of movements, 8 cases(40%) had loss of appetite before treatment. But after treatment only 3 cases(15%) had pain and swelling of PIP joints, 3 cases(15%) had morning stiffness > 1hr, 1 cases(5%) had tenderness, 2 cases(10%) had low grade fever, 3 cases(15%) had arthritis of more than 3 joints, 3 cases(15%) had restriction of movements, 3 cases(15%) had loss of appetite.

GROUP III SUBJECTS (INTERNAL, EXTERNAL MEDICINE AND OTTRADAM):

Among 20 cases, 18 cases(90%) had pain and swelling of PIP joints, 15 cases(75%) had morning stiffness > 1hr, 9 cases(45%) had tenderness, 7 cases(35%) had low grade fever, 19 cases(95%) had arthritis of more than 3 joints, 8 cases(40%) had restriction of movements, 10 cases(50%) had loss of appetite before treatment. But after treatment only 2 cases(10%) had pain and swelling of PIP joints, 1 cases(5%) had morning stiffness > 1hr, 1 cases(5%) had tenderness, 1 cases(5%) had low grade fever, 2 cases(10%) had arthritis of more than 3 joints, 2 cases(10%) had restriction of movements, 2 cases(10%) had loss of appetite.

OVERALL RESULTS:

Among 60 cases, 47 cases(78%) had good improvement, 6 cases(10%) had moderate improvement and 7 cases(12%) had mild improvement.

GRADING OF RESULTS:

There is certainly marked improvement noted in the grading of the result before and after treatment.

STATISTICAL REPORT:

Inference:

Since the p value is significant in all clinical features, so there is significant reducing of clinical features among the patients for the treatment of **Uthiravadha Suronitham (Rheumatoid arthritis)**. Hence it is concluded that the treatment was **effective** and **significant.**

SUMMARY

7. SUMMARY

The primary purpose of the study is to analyse my trial drugs in the disease Uthiravadha Suronitham (Rheumatoid Arthritis).

Many literature reviews in both siddha and modern textbooks has been collected for the disease Uthiravadha Suronitham and Rheumatoid Arthritis respectively. Literature reviews has also been collected from siddha and modern textbooks as well as from various articles for the ingredients in the trial drugs.

The trial drugs Internal and External medicine along with Ottradam has been approved by **Institutional Ethics Committee(IEC No: GSMC-CH-ME-5/011/2016).**

After getting proper permission from the **Institutional Animal Ethics Committee(IAEC No: XLVIII/23/CLBMCP/2016),** Acute and Sub-acute Toxicity for the trial drug SAMUTHARA CHOORANAM was carried out in **Wistar albino rats.**

Standardization and Quality Evaluation(NRS/AS/0084) for the trial drug SAMUTHARA CHOORANAM was carried out in several methods which includes **Organaoleptic characters, Qualitative and Quantitative Analysis, TLC & HPTLC evaluation, Heavy Metal Analysis, Phytochemical analysis and Sterility Test.**

Pharmacological study (Immunomodulator activity) for the trial drug SAMUTHARA CHOORANAM was done in-vitro method by using **RAW 264.7 Cell line.**

The patients with raised **CRP, Anti-CCP**, along with the **clinical symptoms** mentioned in inclusion criteria were included in my clinical trial.

Before conducting the clinical trial, the details about the trial drug and my study was informed to the patients in their vernacular language and their signature were obtained in the consent forms. Separate Proforma was maintained for each and every patient.

After completing all above studies and procedures, the clinical study was conducted in 60 patients. Out of which 20 were treated with Internal medicine (Group I), 20 patients were treated with External medicine with Ottradam(Group II) and 20 patients were treated with Internal and External medicine with Ottradam therapy(Group III)

The trial drugs SAMUTHARA CHOORANAM at the dose of **2 grams (twice daily)** and VADHA NOIKU VELIPRAYOGHA THAILAM of **50ml (per week)** with OTTRADAM were administered to the above said group patients for **48 days.**

The Efficacy of the trial drugs were assessed by Reduction in Inflammation of joints, Morning stiffness, CRP and Anti-CCP.

The Safety of the trial drugs were assessed by comparing the safety parameters LFT & RFT before and after treatment.

Hence the **Statistical Analysis** helps to evaluate the **EFFICACY** and **SAFETY** of the trial drug **SAMUTHARA CHOORANAM(Internal), VADHA NOIKU VELIPRAYOGHA THAILAM(External) with OTTRADAM(Therapy)** in **Uthiravadha Suronitham (Rheumatoid Arthritis)**.

CONCLUSION

8. CONCLUSION

As expressed before, various studies have conducted to evaluate whether the trial drug Samuthara chooranam(Internal) along with Vadha Noiku Veliprayogha Thailam(External) and Ottradam(Therapy) is Efficacy and Safety for the disease Uthiravadha suronitham (Rheumatoid Arthritis).

Heavy Metal Analytical study clearly shows that the metal mercury was absent and the metal arsenic seems very low trace when compared to the allowed recommended limit in the sample Samuthara chooranam. Thus the drug Samuthara chooranam is recommended for the clinical trial.

Phytochemical study indicates the presence of rich Flavanoids, Glycosides, Steroids, Phenol, Tanin, Saponins and Sugar. This analysis clearly proves that the ingredients of Samuthara chooranam has Antioxidant and Immunomodulator activity which helps to reduce the inflammation in RA.

Acute oral toxic study and Repeated dose 28-day oral toxic study was done in Wistar Albino Rats for the sample Samuthara chooranam and hence no other significant changes were observed in their behavior, body weight, water intake, food intake, LFT, RFT. It proves that the trial drug Samuthara chooranam is safe for animal models.

In Pharmacological study, 25µg/ml concentration of Samuthara chooranam has rich level of nitrate(573.21µg) and thus proven to be a potent IMMUNOMODULATOR drug.

Overall clinical study with the trial drugs (Internal, External medicine with Therapy) for 48days reveals that 78% cases have Good improvement, 10% cases have Moderate improvement and 12% cases have mild improvement in patients with Uthiravadha suronitham(RA).

CONCLUSION/2018

This study proves that the trial medicines are more Effective in reducing the signs and symptoms of Uthiravadha suronitham(RA) such as Inflammation of joints (PIP, MCP, Wrist, Ankle), Morning stiffness, Tenderness, Loss of appetite and Restriction of movements.

There is no significant changes in LFT and RFT before and after the treatment. No Adverse reactions has noted in the clinical study. Hence it proves that the trial medicine Samuthara chooranam along with External oil and therapy is safe for human trial.

Finally from all above studies and results, I conclude that my clinical study with siddha trial medicine Herbal – Mineral formulation drug "SAMUTHARA CHOORANAM" (INTERNAL) a potent Immunomodulator, along with "VADHA NOIKU VELIPRAYOGHA THAILAM" (EXTERNAL) and "OTTRADAM" (THERAPY) has been proven to be much EFFICACY and SAFETY for treating the disease UTHIRAVADHA SURONITHAM (RHEUMATOID ARTHRITIS).

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ANNEXURES

GOVERNMENT SIDDHA MEDICAL COLLEGE

Arumbakkam, Chennai-106

Communication Of The Decision Of Institutional Ethics Committee (IEC)

IEC No: GSMC-CH-ME-5/011/2016

Protocol title: AN OPEN COMPARATIVE CLINICAL EVALUATION ON UTHIRAVADHA SURONITHAM (RHEUMATOID ARTHRITIS) WITH SIDDHA HERBAL -MINERAL FORMULATION DRUG "SAMUTHARA CHOORANAM"(INTERNAL) ,"VADHA NOIKU VELIPRAYOGHA THAILAM" (EXTERNAL) & OTTRADAM.
Principal Investigator: Dr. A.B. KAVINAYA
Name & Address of Institution: Government Siddha Medical College, Arumbakkam, Chennai-106
☑ New Review ☐ Revised Review ☐ Expedited Review
Date of review (DD/MM/YY): 05-04-2016 Date of Previous Review, If Revised Application:
Decision of the IEC ☑ Recommended ☐ Recommended with suggestions ☐ Revision ☐ Rejected
Suggestions / Reasons / Remarks: 1. In Inclusion Criteria add duration in morning Stiffness. 2. In Exclusion criteria, add Haemophilia. 3. In Investigations add BT, CT, Serum Uric acid & CRP. Remove RA factor. 4. A Single randomization will be done for trial groups.
Recommended for a period of 1 year from date of completion of preclinical studies :

Please Note:

- Inform IEC immediately in case of any adverse events/serious drug reaction.
- Seek IECapproval in case of any change in the study procedure, site and investigator
- This approval is valid only for period mentioned above
- IEC member have the right to review the trial with prior intimation.

5/4/16

Dr.P.Jeyaprakashnarayanan, M.D(s)
Chairman

Dr.K.Kanakavalli, M.D(s)
Member Secretary

INSTITUTIONAL ETHICS COMMITTEE

Date : 05.04.2016
Sub : IEC review of research proposals.
Ref : Your letter dated

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Dr.R.VASUDEVAN, M.D(S)., PG.DIP (Clinical research), Msc (Medical sociology) Sociologist	✓	
Dr.L.MUKUNTHAN, M.B.B.S., DNB (Medicine)., Modern Medicine Specialist	✓	
Dr. JOSEPH MARIYA ADAIKKALAM,M.D(S)., Msc epidemiology., Social scientist	✓	
Dr.G.AADINATH REDDY, M.Pharm, Ph,D., Biomedical scientist	✓	05/04/16
Mr.B.PADMANABHA PILLAI Philosopher	✓	
Mrs. PREETHA SARAVANAN Public person	✓	05/04/16

Dr. P. Jeyaprakashnarayanan, M.D(s)
Chairman

Dr.K. Kanakavalli, M.D(s)
Member secretary

The Tamil Nadu Dr.M.G.R.Medical University

69, Anna Salai, Guindy, Chennai - 600 032.

This Certificate is awarded to Dr/Mr/Mrs.....A.B. KAVINAYA.....

For participating as ~~Resource~~ ~~Person~~ / Delegate in the Twentieth Workshop on

"RESEARCH METHODOLOGY & BIOSTATISTICS"

*For **AYUSH Post Graduates & Researchers***

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University From 07th to 11th March 2016.

Dr.N.KABILAN, M.D.(S)
PROF & HEAD
DEPT.OF SIDDHA

Prof.**Dr.P.ARUMUGAM,** M.D.,
REGISTRAR i/c

Prof. **Dr.S.GEETHALAKSHMI,** M.D., Ph.D.,
VICE CHANCELLOR

Government Siddha Medical College
Department of Medicinal Botany

Dr. S. Sankaranarayanan M.Sc., M.Phil., Ph.D.,
Asst. Professor
Head of the Department

6, Anna Arch Rd,
NSK Nagar,
Arumbakkam, Chennai,
Tamil Nadu 600106.

AUTHENTICATION CERTIFICATE

Based upon the organoleptic/macroscopic/microscopic examination of fresh/market sample, it is certified that the specimen given to Dr. A. B. Kavinaya B.S.M.S, doing M.D. (S) at Government Siddha Medical College, Arumbakkam, Chennai-106 is identified below as

Binomial name	Family	Voucher Specimen No
Trachyspermum ammi	Apiaceae	GSMC/MB-72/17
Terminalia chebula	Combretaceae	GSMC/MB-73/17
Piper longum	Piperaceae	GSMC/MB-74/17
Zingiber officinale	Zingiberaceae	GSMC/MB-75/17
Ferula asafoetida	Apiaceae	GSMC/MB-76/17
Embelia ribes	Myrsinaceae	GSMC/MB-77/17

References: Flora of Presidency, Gamble, J. S

Date: 01.06.2017

Dr. S. Sankaranarayanan M.Sc., M.Phil., Ph.D.,

Head
Dept. of Maruthuva Thavaraiyal
(Medicinal Botany and Pharmacognosy)
Govt. Siddha Medical College,
Arumbakkam, Chennai - 600 106.

Post Graduate Department of Gunapadam

(Pharmacology)

Government Siddha Medical College, Chennai-106

IDENTIFICATION AND AUTHENTICATION CERTIFICATE

NAME OF THE STUDENT : A.B. KAVINAYA

DEPARTMENT : PG - SIRAPPU MARUTHUVAM

BATCH YEAR : 2015 - 2018

NAME OF THE SAMPLE : INDUPPU (Rocksalt), YAVACHARAM (Potassium carbonate)
KALUPPU (SODIUM CHLORIDE IMPURA)

SAMPLE DESCRIPTION : Dried whole plant / Metal / Mineral ✓

DATE OF THE RECEIPT : 06/06/17

REPORT

This sample has been critically studied with macroscopic and organoleptic characters along with relevant literature, I declared that this Plant/Metal/Mineral material is correctly identified as .INDUPPU., YAVACHARAM., KALUPPU..... and I hereby authenticate the sample given by .Dr. A.B. KAVINAYA..

This certificate issued at his/her request and is given only for dissertation purpose.

Date: 6.6.2017

Place: Chennai

Dr.SARAVANADEVI, MD(S)
PG HOD of Gunapadam

Head of the Department
Gunapadam
Govt. Siddha Medical College,
CHENNAI-600 106.

C.L.BAID METHA COLLEGE OF PHARMACY

(An ISO 9001-2000 certified institute)

Jyothi Nagar, Old Mahabalipuram Road

Thoraipakkam, Chennai – 600 097

CERTIFICATE

This is to certify that the project entitled, Toxicological study on **SAMUTHARA CHOORANAM** in rats submitted in partial fulfilment for the degree of M.D. (siddha) was carried out at C.L. Baid Metha college of Pharmacy, Chennai-97, in the Department of Pharmacology during the academic year of 2016-2017. It has been approved by the IAEC No: XLVIII/23/CLBMCP/2016

C.L. Baid Metha College of Pharmacy CHENNAI-97 Thoraipakkam

Dr.P.Muralidharan

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E-mail : nobleresearchsolutions@gmail.com
info@nobleresearchsolutions.com
Contact : 9710437419, Admin : 044 - 42691289

Date: 22.07.2017

To,

Dr.A.B.Kavinaya

Govt Siddha Medical College,

Arumbakkam, Chennai, Tamil Nadu- 600106, India

Project Id: **NRS/AS/0084**

This is to certify that Dr.A.B.Kavinaya from Govt Siddha Medical College, Arumbakkam, Chennai, has carried out the following activity at our facility for the trial drug *Samuthara Chooranam (SC)*

The list of activities are as follows

- *Phytochemical Analysis*
- *Heavy Metal Analysis*
- *HPTLC*
- *TLC*
- *Sterility Evaluation*
- *Physicochemical Evaluation*

Note: Annexures was attached as a separate enclosure along with this report.

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E-mail: nobleresearchsolutions@gmail.com
Contact: 9710437419, Admin: 044 - 42691289

Project ID	NRS/AS/0084/01/2018
Name and Address of the Researcher	DR.A.B.Kavinaya Govt Siddha Medical College, Chennai Tamil Nadu, India
Parameter Requested by the Customer for Analysis	Heavy Metal analysis by AAS
Sample Received	Post
Sample –ID	SC
Description of the Sample	Solid
Method of Analysis Instrument Extraction Solvent	 Model: AA 240 Series HCl
Analysis Type	Third Party Analysis
Date of Analysis	07/02/2018
Result of Analysis	Test Report Attached

E-mail: nobleresearchsolutions@gmail.com
Contact: 9710437419, Admin: 044 - 42691289

HEAVY METAL ANALYSIS BY AAS

Standard: Hg and As- Sigma

Methodology

Atomic Absorption Spectrometry (AAS) is a very common and reliable technique for detecting metals and metalloids in environmental samples. The total heavy metal content of the sample SC was performed by Atomic Absorption Spectrometry (AAS) Model AA 240 Series. In order to determination the heavy metals such as mercury and arsenic concentrations in the test sample SC

Sample Digestion

Test sample SC digested with 1mol/L HCl for determination of arsenic and mercury.

Standard reparation

As & Hg- 100 ppm sample in 1mol/L HCl

Test Report of the Sample SC

Name of the Heavy Metal	Absorption Max Λ max	Result Analysis	Maximum Limit
Mercury	253.7 nm	BDL	1 ppm
Arsenic	193.7 nm	0.268 ppm	3 ppm

BDL- Below Detection Limit

Report and Inference

- Results of the present investigation has clearly shows that the sample SC has no traces of Mercury and further shows the presence of Arsenic at 0.268 ppm level and hence it was considered that the heavy metals mercury was absent in the sample SC.
- The reported heavy metal arsenic seems very low (0.268 ppm) when compare to the allowed recommended limit of 3ppm.

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Project ID	NRS/AS/0084/01/2018
Name and Address of the Researcher	DR.A.B.Kavinaya Govt Siddha Medical College, Chennai Tamil Nadu, India
Parameter Requested by the Customer for Analysis	HPTLC Analysis
Sample Received	Post
Sample –ID	SC
Description of the Sample	Solid
Method of Analysis Instrument TLC Plate Mobile Phase Extraction Solvent	 CAMAG TLC SCANNER III Aluminium Coated Silica Gel – Merck Toulene: Ethyl Acetate: Acetic Acid (1.5:1:0.5) Acetone
Analysis Type	Third Party Analysis
Date of Analysis	30/01/2018
Result of Analysis	Test Report Attached

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TLC Analysis at 254 nm

TLC Analysis at 366 nm

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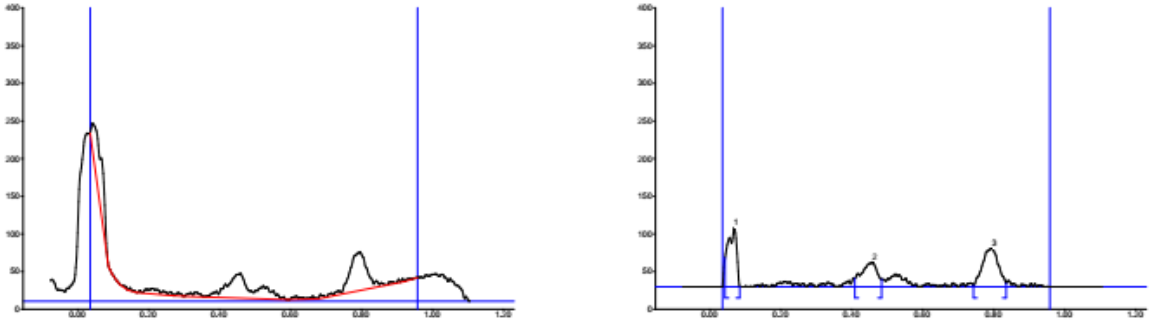
Contact: 9710437419, Admin: 044 - 42691289

HPTLC finger printing of Sample SC



Peak Table

Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %
1	0.04	39.0	0.07	78.7	48.29	0.08	0.4	1461.7	33.99
2	0.41	11.3	0.46	33.0	20.28	0.48	10.2	1089.4	25.33
3	0.74	2.4	0.80	51.2	31.43	0.84	5.0	1749.9	40.69

REPORT

HPTLC finger printing analysis of the sample SC reveals the presence of three prominent peaks corresponds to presence of three versatile phytocomponents present with in it. Rf value of the peaks ranges from 0.04 to 0.74. Further the peak 1 occupies the major percentage of area of 48.29 % which denotes the abundant existence of such compound. Followed by this peak 3 and 2 occupies the percentage area of 31.43 and 20.28 %.

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Project ID	NRS/AS/0083/01/2018
Name and Address of the Researcher	Dr.A.B.Kavinaya Department of Special Medicine Govt Siddha Medical College, Chennai Tamil Nadu, India
Parameter Requested by the Customer for Analysis	Physicochemical Analysis
Sample Received	Post
Sample –ID	Samuthata Chooranam SC
Description of the Sample	Solid
Method of Analysis	PLIM- Protocol – ASU Formulations
Analysis Type	Physicochemical Analysis
Date of Analysis	02/03/2018
Result of Analysis	Test and Analytical Reports Attached As Annexures

Test Report

S.NO	TEST	OBSERVATION
1	ALKALOIDS	-
2	FLAVANOIDS	+
3	GLYCOSIDES	+
4	STEROIDS	+
5	TRITERPENOIDS	-
6	COUMARIN	-
7	PHENOL	+
8	TANIN	+
9	PROTEIN	-
10	SAPONINS	+
11	SUGAR	+
12	ANTHOCYANIN	-
13	BETACYANIN	-

Note: +-> Indicates Presence and - -> Indicates Absence of the Phytocomponents.

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POST GRADUATE DEPARTMENT OF SIRAPPU MARUTHUVAM

AN OPEN COMPARATIVE CLINICAL EVALUATION ON **UTHIRAVADHA SURONITHAM (RHEUMATOID ARTHRITIS)** WITH SIDDHA HERBAL-MINERAL FORMULATION DRUG **"SAMUTHARA CHOORANAM"(INT), "VADHA NOIKU VELIPRAYOGHA THAILAM" (EXT)** AND **OTTRADAM"**

FORM l - SCREENING AND SELECTION PROFORMA

1. OP NO: .....

2. NAME: …….

3. AGE&GENDER: ……..... 4.OCCUPATION:……

5.INCOME: ……

6. ADDRESS: ……

……

……

7. CONTACT NO: ……

INCLUSION CRITERIA

- Age: 18-60 Years YES/NO
- Sex: Both male & female YES/NO
- Low grade fever YES/NO
- Pain,swelling & tenderness in interphalangeal joints YES/NO
- Pain and swelling in other joints YES/NO
- Redness of joint YES/NO
- Morning stiffness YES/NO
- Anti CCP +ve YES/NO
- CRP +ve YES/NO
- RA factor +ve /-ve YES/NO

- Arthritis of 3 or more joints YES/NO
- Patient willing to sign the consent form. YES/NO

EXCLUSION CRITERIA

KNOWN CASES OF

- Rheumatic fever
- Psoriatic arthropathica
- Gouty arthritis
- Systemic lupus erythematosus(SLE)
- Progressive systemic sclerosis(PSS)
- History of long term intake of steroids
- Renal failure
- Carries spine
- Ankylosing spondylitis
- Tumours
- Osteomyelitis
- HIV
- Pregnancy and lactation

ADMITTED TO TRIAL:

YES **NO**

If yes, **OPD**

Date:

Station:

Signature of the Guide Signature of the Investigator

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FORM lI -HISTORY TAKING PROFORMA

1. SERIAL NO OF THE CASE: ……. 2.OP/IP NO:…….

3. NAME: …… 4. AGE & GENDER ……

6. OCCUPATION: …… 7. INCOME:……

8.COMPLAINTS & DURATION:

9. CHIEF COMPLAINTS WITH DURATION

	Present	**Absent**
• Low grade fever		
• Pain in the joints		
• Tenderness & Swelling of joints		
I. MCP		
II. PIP		
III. Wrist		
IV. Ankle		
V. Knee		
• Morning stiffness		
• Restriction of joint movements		

- Loss of appetite
- Subcutaneous nodules
- Ulnar deviation
- Deformities

HISTORY OF PRESENT ILLNESS

1. **Onset of disease** **:** Acute Insidious
2. **Duration of disease** **:**
3. **Treatment given so far** **:** Ayurvedic medicine Modern Medicine

   Unani Homeopathy

8.PERSONAL HISTORY:

PERSONAL HABITS	YES	NO	IF YES, SPECIFY DURATION/QUANTITY
Smoking			
Tobacco Chewing			
Alcoholism			
Narcotic drugs			

9. HISTORY OF PREVIOUS ILLNESS/PELVIC SURGERY

10. DIETARY HABIT:

1.Vegetarian

2.Non-vegetarian

11. FAMILY HISTORY:

Whether this problem runs in family?

1. Yes 2.No

If yes, mention the relationship of affected person(s) ----------

History of previous investigations if any ----------

Date:

Station:

Signature of the Guide Signature of the Investigator

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FORM III

CLINICAL ASSESSMENT ON ENROLLMENT AND ON VISITS

1. SI NO:..... 2. OP NO: ---------- 3. NAME:.....

4. RELIGION: H / C / M / O

5. AGE/GENDER:..... 6. OCCUPATION: ……

7. SOCIAL STATUS:……. 8.CONTACT NUM:……

SIDDHA SYSTEM OF EXAMINATION

1. THEGI (BODY CONSTITUTION):

1. Vatha udal ☐
2. Pitha udal ☐
3. Kaba udal ☐
4. Thontha udal ☐

2. NILAM (LAND WHERE THE PATIENT LIVED MOST):

1. Kurinji ☐
2. Mullai ☐
3. Marutham ☐
4. Neithal ☐
5. Paalai ☐

3. KAALAM:

1. Kaar kaalam (Aavani-Puratasi) ☐
2. Koothir kaalam (Ippasi-Kaarthigai) ☐
3. Munpani kaalam (Maargazhi-Tai) ☐
4. Pinpani kaalam (Maasi-Panguni) ☐
5. Ilavenil kaalam (Chithirai-Vaigasi) ☐
6. Muthuvenil kaalam (Aani-Aadi) ☐

4. GUNAM:

1. Sathuvam ☐
2. Rasatham ☐
3. Thamasam ☐

5. PORI PULANGAL (SENSORY ORGANS):

	Normal	**Affected**	
1. Mei	☐	☐	.....
2. Vaai(Naaku)	☐	☐	.....
3. Kan	☐	☐	.....
4. Mookku	☐	☐	.....
5. Sevi	☐	☐	.....

6. KANMENDRIYAM (MOTOR ORGANS) :

	Normal	**Affected**	
1. Vaai	☐	☐	.....
2. Kaal	☐	☐	.....
3. Kai	☐	☐	.....
4. Eruvaai	☐	☐	.....
5. Karuvaai	☐	☐	.....

7. KOSANGAL (SHEATH):

	Normal	**Affected**	
1. Annamaya kosam	☐	☐	.....
2. Pranamaya kosam	☐	☐	.....
3. Manomaya kosam	☐	☐	.....

4. Vignanamaya kosam ☐ ☐ .....

5. Anandhamaya kosam ☐ ☐ .....

8. UYIR THATHUKKAL (THREE HUMOURS):

8a.VALI:	**Normal**	**Affected**	
1. Praanan	☐	☐	……
2. Abaanan	☐	☐	.....
3. Viyaanan	☐	☐	.....
4. Uthaanan	☐	☐	.....
5. Samaanan	☐	☐	.....
6. Naagan	☐	☐	.....
7. Koorman	☐	☐	.....
8. Kirukaran	☐	☐	.....
9. Devathathan	☐	☐	.....
10. Dhananjayan	☐	☐	……..

8b. AZHAL:	**Normal**	**Affected**	
1. Analam	☐	☐	……
2. Ranjagam	☐	☐	.....
3. Saathagam	☐	☐	.....
4. Aalosagam	☐	☐	.....
5. Praasagam	☐	☐	.....

8c.IYAM:	**Normal**	**Affected**	
1. Avalambagam	☐	☐	.....
2. Kilethagam	☐	☐	.....
3. Pothagam	☐	☐	.....
4. Tharpagam	☐	☐	.....
5. Santhigam	☐	☐	.....

9. EN VAGAI THERVU (EIGHT FOLDS OF EXAMINATION):

1.Naadi : …….....

2.Parisam : …….....

3.Naa : .....…….....

4.Niram : .....…….....

5.Mozhi : .....…….....

6.Vizhi : .....

7.Malam : .....

8. Moothiram : …….

8a.Neerkuri:

Niram : 1.Whitish ☐ 2. Yellowish ☐

3.Straw coloured ☐ 4. Crystal clear ☐

Edai: 1.Present ☐ 2.Absent ☐

Manam : 1.Nil ☐ 2.Reduced ☐ 3. Increased ☐

Nurai: 1. Normal ☐ 2. Increased ☐ 3. Decreased ☐

Enjal:

8b: Neerkuri (Oil –in urine sign):

Vatha Neer ☐ Pitha Neer ☐ Kaba Neer ☐

10. SEVEN UDAL THAATHUKKAL (SEVEN SOMATIC COMPONENTS):

	Normal	**Affected**	
1. Saaram	☐	☐	……
2. Senneer	☐	☐	……
3. Oon	☐	☐	……
4. Kozhuppu	☐	☐	……
5. Enbu	☐	☐	.....
6.Moolai	☐	☐	.....
7. Sukkilam / Suronitham	☐	☐	.....

GENERAL EXAMINATION:

1. Body weight [Kg] :
2. Height [cm] :
3. Body Temperature [F] :
4. Blood Pressure (mmHg) :
5. Pulse Rate /min. :

6. Heart Rate / min. :
7. Respiratory Rate /min. :

		Yes	No
8. Pallor	:	☐	☐
9. Jaundice	:	☐	☐
10. Clubbing	:	☐	☐
11. Cyanosis	:	☐	☐
12. Pedal Oedema	:	☐	☐
13. Lymphadenopathy	:	☐	☐
14. Jugular venous pulsation	:	☐	☐

VITAL ORGAN EXAMINATION:

	Normal	Abnormal
1. Heart	☐	☐
2. Lungs	☐	☐
3. Brain	☐	☐
4. Liver	☐	☐
5. Kidney	☐	☐
6. Spleen	☐	☐
7. Stomach	☐	☐

SYSTEMIC EXAMINATION:

	Normal	Abnormal
1. Cardio-vascular system	☐	☐
2. Respiratory system	☐	☐
3. Gastro intestinal system	☐	☐
4. Central nervous system	☐	☐
5. Genital urinary system	☐	☐
6. Endocrine system	☐	☐

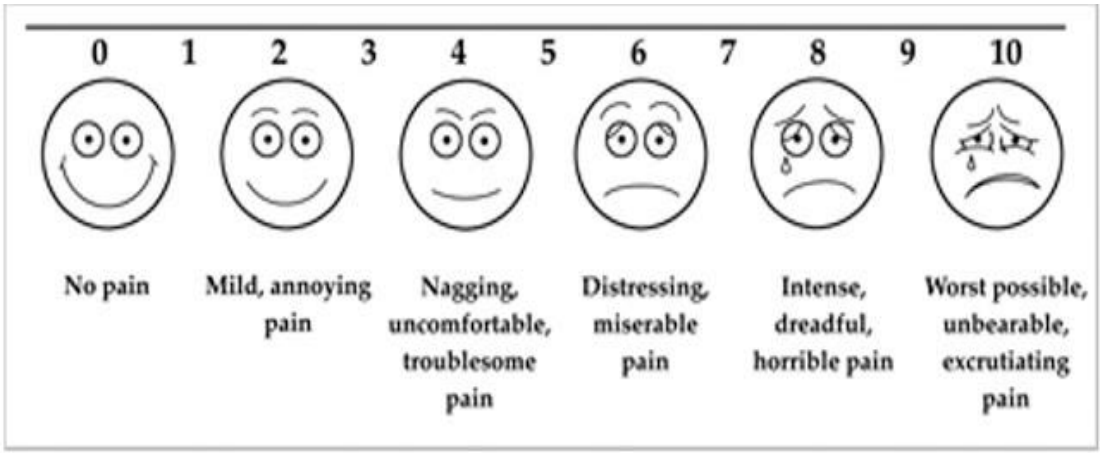
CLINICAL ASSESSMENT AND PROGRESS

S.NO	CLINICAL FEATURES	BEFORE TREATMENT	AFTER TREATMENT					
			8th DAY	16th DAY	24th DAY	32nd DAY	40th DAY	48th DAY
1.	Pain in the joints							
2.	Morning stiffness							
3.	Swelling and Tenderness of joints a. PIP							
	b. MCP							
	c. Wrist							
	d. Ankle							
	e. Knee							
4.	Fever							
5.	Loss of appetite							
6.	Anaemia							
7.	Restriction of joint							
8.	Subcutaneous nodules							
9.	Ulnar deviation							
10.	Deformities							

0 – nil
+ - mild
++ - moderate
+++ - severe

PAIN ASSESMENT:

VISUAL ANALOGUE SCALE;



Date :

Station:

Signature of the Guide

Signature of the Investigator

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POST- GRADUATE DEPARTMENT OF SIRAPPU MARUTHUVAM

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FORM IV: LABORATORY INVESTIGATIONS PROFORMA

1. SERIAL NO OF THE CASE: …… 2.OP NO:……..

3. NAME: …….. 4.AGE & GENDER: .....

A) BLOOD INVESTIGATIONS:

BLOOD INVESTIGATIONS		**BEFORE TREATMENT**	**AFTER TREATMENT**
Hb (gm/dL)			
ESR (mm)	**½ hr.**		
	1 hr.		
T.WBC (Cells / Cu.mm)			
Differential Count (%)	**Polymorphs**		
	Lymphocytes		
	Monocytes		
	Eosinophils		
	Basophils		

BLOOD INVESTIGATIONS		BEFORE TREATMENT	AFTER TREATMENT
Blood glucose (mg/dl)	**Fasting**		
	PP		
Serum Uric acid (mg/dl)			
Bleeding time			
Clotting time			
Renal Function Test	**Blood urea(mg/dl)**		
	Serum creatinine(mg/dl)		
Liver function test	**Alkaline phosphatase(U/L)** **SGOT(U/L)** **SGPT(U/L)**		
Specific Investigation	**CRP (mg/dl)** **Anti CCP (U/ml)**		

B) URINE INVESTIGATIONS:

URINE INVESTIGATIONS	BEFORE TREATMENT	AFTER TREATMENT
Albumin		
Sugar		
Deposits		

Date:

Station:

Signature of the Guide

Signature of the Investigator

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CHENNAI – 600 106

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FORM V: INFORMED CONSENT FORM

*"**I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any question I have asked has been answered to my satisfaction.***

***I consent voluntarily to participate as a participant in this study and understand that I have the right to withdraw from the study at any time without in any way it affecting my further medical care**".*

"I have received a copy of the information sheet/consent form".

Date:

Signature of the Participant Signature of the Investigator

In case of Illiterate Participant

*"**I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely**."*

Date:

Signature of a witness

(Selected by the participant bearing no connection with the Survey team) Left thumb Impression

Date: of the Participant

Station:

Signature of the Investigator

Signature of the Participant

Signature of the Guide

அரசு சித்த மருத்துவக் கல்லூரி, சென்னை-106

அறிஞர் அண்ணா மருத்துவமனை, சென்னை

உதிரவாத சுரோணிதம் நோய்க்கான சித்தமருந்தின் "சாமுதர சூரணம்,

வாத நோய்க்கு வெளிப்பிரயோக தைலம் மற்றும் ஒற்றடம்)

பரிகரிப்புத் திறணைக் கண்டரியும் மருத்துவ ஆய்விற்கான தகவல் படிவம்

ஒப்புதல் படிவம் ஆய்வாளரால் சான்றளிக்கப்பட்டது

நான் இந்த ஆய்வை குறித்த அனைத்து விபரங்களையும் நோயாளிக்கு புரியும் வகையில் எடுத்துரைத்தேன் என உறுதியளிக்கிறேன்.

தேதி: கையெப்பம்

இடம்: பெயர்:

நோயாளியின் ஒப்புதல் படிவம்

என்னிடம் இந்த மருத்துவ ஆய்வின் காரணத்தையும், மருந்தின் தன்மை மற்றும் மருத்துவ வழிமுறை பற்றியும், தொடர்ந்து எனது உடல் இயக்கத்தை கண்காணிக்கவும், அதனை பாதுகாக்கவும் பயன்படும் மருத்துவ ஆய்வுக்கூட பரிசோதனைகள் பற்றி திருப்தி அளிக்கும் வகையில் ஆய்வு மருத்துவரால் விளக்கிக் கூறப்பட்டது.

நான் இந்த மருத்துவ ஆய்வின் போது, காரணம் எதுவும் கூறாமல், எப்பொழுது வேண்டுமானாலும் இந்த ஆய்விலிருந்து என்னை விடுவித்து கொள்ளும் உரிமையை தெரிந்திருக்கின்றேன். நான் என்னுடைய சுதந்திரமாக தேர்வு செய்யும் உரிமையைக் கொண்டு உதிரவாத சுரோணிதம் நோய்க்கான சாமுதர சூரணம் மருந்தின் பரிகரிப்புத் திறணைக் கண்டரியும் மருத்துவ ஆய்விற்கு என்னை உட்படுத்த ஒப்புதல் அளிக்கிறேன்.

தேதி: கையெப்பம்

இடம்: பெயர்:

தேதி:

இடம்:

உறவுமுறை:

சாட்சிக்காரர் கையெப்பம்

பெயர்:

துறைத்தலைவர் கையெப்பம்

ஆராய்ச்சியாளர் கையெப்பம்

GOVERNMENT SIDDHA MEDICAL COLLEGE,

ARIGNAR ANNA GOVERNMENT HOSPITAL OF INDIAN MEDICINE

CHENNAI – 600 106

AN OPEN COMPARATIVE CLINICAL EVALUATION ON **UTHIRAVADHA SURONITHAM (RHEUMATOID ARTHRITIS)** WITH SIDDHA HERBAL-MINERAL FORMULATION DRUG **"SAMUTHARA CHOORANAM"(INT), "VADHA NOIKU VELIPRAYOGHA THAILAM" (EXT)** AND **OTTRADAM"**

FORM VI - WITHDRAWAL FORM

SI NO: **OP NO:**

NAME: **AGE / GENDER :**

DATE OF TRIAL COMMENCEMENT:

DATE OF WITHDRAWAL FROM TRIAL:

REASONS FOR WITHDRAWAL:

- Long absence at reporting : Yes/ No
- Irregular treatment: Yes/ No
- Shift of locality : Yes/No
- Increase in severity of symptoms: Yes/No
- Development of severe adverse drug reactions: Yes/No

Date:

Station:

Signature of the Guide Signature of the Investigator

GOVERNMENT SIDDHA MEDICAL COLLEGE

ARIGNAR ANNA GOVERNMENT HOSPITAL OF INDIAN MEDICINE

CHENNAI – 600 106

POST GRADUATE DEPARTMENT OF SIRAPPU MARUTHUVAM

AN OPEN COMPARATIVE CLINICAL EVALUATION ON **UTHIRAVADHA SURONITHAM (RHEUMATOID ARTHRITIS)** WITH SIDDHA HERBAL-MINERAL FORMULATION DRUG **"SAMUTHARA CHOORANAM"(INT), "VADHA NOIKU VELIPRAYOGHA THAILAM" (EXT)** AND **OTTRADAM"**

FORM VII – PATIENT INFORMATION SHEET

Name of Investigator: Dr.A.B.KAVINAYA

Name of the college: Govt. Siddha Medical College
Arumbakkam
Chennai-106.

INFORMATION SHEET FOR PATIENTS PARTICIPATING IN THE OPEN CLINICAL TRIAL.

I, A. B. KAVINAYA studying M.D (Siddha) at Govt. Siddha Medical College, Chennai, is doing a clinical trial on **"Uthiravadha suronitham(Rheumatoid arthritis)"**. It is becoming a most common disease, occurring throughout the world. In this regard, I am in need to ask you few questions. I will maintain confidentiality of your comments and data obtained. There will be no risk of disclosing your identity and no physical, psychological or professional risk is involved by taking part in this study. Taking part in this study is voluntary. No compensation will be paid to you for taking part in this study.

You can choose not to take part. You can choose not to answer a specific question. There is no specific benefit for you if you take part in the study. However, taking part in the study may be of benefit to the community, as it may help us to understand the problem of defaulters and potential solutions.

If you agree to be a participant in this study, you will be included in the study primarily by signing the consent form and then you will be given the internal medicine "**SAMUTHARA CHOORANAM**" (Internal medicine) Two gram bid with Ghee for 48 days.

The information I am collecting in this study will remain between you and the Co- investigator (myself). I will ask you few questions through a questionnaire. I will not write your name on this form. I will use a code instead.

The questionnaire will take approximately 20 minutes of your time.

If you wish to find out more about this study before taking part, you can ask me all the questions you want or contact A.B.KAVINAYA, PG Scholar cum co-investigator of this study, attached to Govt. Siddha Medical College, Chennai-106. You can also contact the Member-secretary of Ethics committee, Govt. Siddha Medical College, Chennai.

அரசு சித்த மருத்துவக் கல்லூரி, சென்னை-106

அறிஞர் அண்ணா மருத்துவமனை, சென்னை

உதிரவாத சுரோணிதம் நோய்க்கான சித்த மருந்தின் "சாமுதர சூரணம், வாத நோய்க்கு வெளிப்பிரயோக தைலம் மற்றும் ஒற்றடம்" பரிகரிப்புத் திறணைக் கண்டரியும் மருத்துவ ஆய்விற்கான தகவல் படிவம்

ஆராய்ச்சியாளர் பெயர்: ஆ.பூ.கவிநயா

நிறுவனத்தின் பெயர்: அரசு சித்த மருத்துவக் கல்லூரி,
அரும்பாக்கம்
சென்னை-106

அரசு சித்த மருத்துவக் கல்லூரியில் பட்ட மேற்படிப்பு பயின்று வரும் நான் மருத்துவர் ஆ.பூ.கவிநயா, உதிரவாத சுரோணிதம் என்னும் நோயில் மருத்துவ ஆராய்ச்ச்யில் ஈடுபட்டுள்ளேன்.

இந்த ஆராய்ச்சி சம்பந்தமான சில கேள்விகளைக் கேட்கவும், தேவையான பரிசோதனைக்கு தங்களை உட்படுத்தவும் உள்ளேன்.

இந்த ஆராய்ச்சிக்கு தாங்கள் விருப்பத்தின் பேரில் உட்படும் பட்சத்தில் உள்மருந்தாக "சாமுதர சூரணம்" 2 கிராம் நெய்யில் இருவேளை(காலை, மாலை) உணவுக்கு பின் 48 நாட்கள் உட்கொள்ள வேண்டும். வெளிமருந்தாக "வாத நோய்க்கு வெளிப்பிரயோக தைலம்" 48 நாட்கள் நோய் உள்ள இடங்களில் வெளியே தடவி ஒற்றடம் செய்ய வேண்டும். வெளி நோயாளர்கள் 7 நாட்களுக்கு ஒருமுறை மருத்துவமனைக்கு வர வேண்டும்.

இந்த ஆராய்ச்சியில் தங்களை அனுமதித்த பிறகு உங்களுக்கு விருப்பம் இல்லையெனில் எப்போது வேண்டுமானாலும் ஆராய்ச்சியில் இருந்து விலகிக் கொள்ள உரிமை உள்ளது.

இந்த ஆராய்ச்சி சம்மந்தமாக நோயின் தன்மை பற்றியும் மற்ற விபரங்களுக்கும் ஆராய்ச்சியாளரான மருத்துவர் ஆ.பூ.கவிநயா(பட்ட மேற்படிப்பாளர் சிறப்பு மருத்துவ துறை) அவர்களை எந்த நேரத்திலும் தொடர்பு

கொள்ளலாம். கைபேசி எண்:7502469757

மேலும் இந்த ஆராய்ச்சிக்கு தக்க அனுமதி சான்று(IEC) பெறப்பட்டு உள்ளது.

மேலும் உணவு முறையில் மருத்துவரால் கூறப்படும் பத்தியம் காக்குமாறு அறிவுறுத்தபடுகிறது.

இது சம்பந்தமான தங்களது அனைத்து விபரங்களும் ரகசியமாக வைக்கப்படும் என உறுதி அளிக்கிறேன்.

இதில் பயணப்படி முதலிய எந்த உதவித் தொகையும் வழங்கப்பட மாட்டாது.

இந்த ஆராய்ச்சியின் போது உடலுக்கு வேறு பாதிப்பு ஏற்படும் பட்சத்தில் அறிஞர் அண்ணா சித்த மருத்துவமனையில் தக்க சிகிச்சை அளிக்கப்படும்.

இந்த மருந்து சிறப்பாக உதிரவாத சுரோணிதம் நோய்க்காக அங்கீகரிக்கப்பட்ட சித்த மருத்துவ நூலில் கூறப்பட்டுள்ளது. ஏற்கனவே உபயோகத்தில் உள்ள இதுபோன்ற மருந்து இதுவரை நோயாளிகளிடம் எந்தவித பக்கவிளைவுகளை ஏற்படுத்தவில்லை.

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FORM VIII: DIETARY ADVICE FORM

சேர்க்க கூடிய உணவுகள்:

- **காய்கள்: கத்திரி பிஞ்சு, முருங்கை பிஞ்சு, அவரை பிஞ்சு ஆகியவை சேர்க்க வேண்டும்.**
- **கீரைகள்: கரிசாலை, பொன்னாங்கன்னி,ம ணத்தக்காளி, முருங்கைகீரை, பசலைக்கீரை, சிறுகீரை, கறிவேப்பிலை ஆகியவை சேர்க்க வேண்டும்.**
- **பழங்கள்: மாதுளை, ஆப்பில், வாழை, பேரீச்சை, அத்தி, திராச்சை, கொய்யா, ஆரஞ்சு, எலிமிச்சை, நாவல், தக்காளி ஆகியவை சேர்க்க வேண்டும்.**
- **தானியங்கள்: கோதுமை, ஓட்ஸ், சோயாபீன்ஸ், பட்டாணி, கொண்டைகடலை, எள், பாதாம் ஆகியவை சேர்க்க வேண்டும்.**
- **அசைவம்: வெள்ளாட்டுக்கறி, ஈரல், எலும்புமஜ்ஜை ஆகியவை சேர்க்க வேண்டும்.**

சேர்க்க கூடாதவைகள்:

- **மந்தப்பொருள்**
- **ஊருளைக் கிழங்கு**
- **அகத்திக்கீரை**
- **புளிப்பு**
- **புகையிலை**
- **மது அருந்துதல்**

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FORM IX: ADVERSE REACTION FORM

SERIAL NO:

OP NO:

NAME:

AGE/GENDER:

DATE OF TRIAL COMMENCEMENT:

DATE OF OCCURENCE OF THE ADVERSE REACTION:

TIME

DESCRIPTION OF ADVERSE REACTION:

Date:

Station:

Signature of the Guide **Signature of the Investigator**